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DICTIONARY FILE UPDATES:  31 JAN 2007  HIGHEST RN 918932-71-5

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L5              STR
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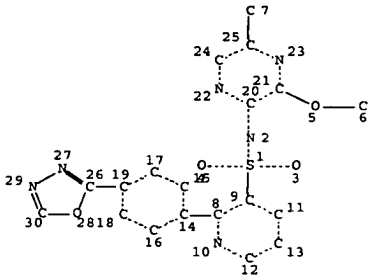

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  30

STEREO ATTRIBUTES: NONE
L7            1 SEA FILE=REGISTRY FAM FUL L5

100.0% PROCESSED       1 ITERATIONS                     1 ANSWERS
SEARCH TIME: 00.00.01
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=> d ide l7

L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   186497-07-4  REGISTRY
ED   Entered STN:  27 Feb 1997
CN   3-Pyridinesulfonamide, N-(3-methoxy-5-methylpyrazinyl)-2-[4-(1,3,4-
     oxadiazol-2-yl)phenyl]- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   ZD 4054
CN   Zibotentan
MF   C19 H16 N6 O4 S
SR   CA
LC   STN Files:   CA, CAPLUS, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, SYNTHLINE,
       TOXCENTER, USPATFULL
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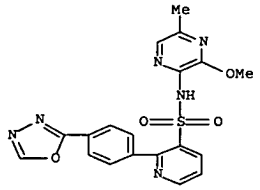

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             15 REFERENCES IN FILE CA (1907 TO DATE)
             15 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> fil capl uspatf toxcenter imsdrugnew imsres prousddr synthline; s l7
FILE 'CAPLUS' ENTERED AT 16:09:33 ON 01 FEB 2007
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FILE 'USPATFULL' ENTERED AT 16:09:33 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE 'IMSDRUGNEWS' ENTERED AT 16:09:33 ON 01 FEB 2007
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FILE 'IMSRESEARCH' ENTERED AT 16:09:33 ON 01 FEB 2007
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FILE 'PROUSDDR' ENTERED AT 16:09:33 ON 01 FEB 2007
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FILE 'SYNTHLINE' ENTERED AT 16:09:33 ON 01 FEB 2007
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L8          46 L7

=> dup rem l8
DUPLICATE IS NOT AVAILABLE IN 'IMSRESEARCH, PROUSDDR, SYNTHLINE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L8
L9           35 DUP REM L8 (11 DUPLICATES REMOVED)
                ANSWERS '1-15' FROM FILE CAPLUS
                ANSWERS '16-25' FROM FILE USPATFULL
                ANSWERS '26-32' FROM FILE IMSDRUGNEWS
                ANSWER '33' FROM FILE IMSRESEARCH
                ANSWER '34' FROM FILE PROUSDDR
                ANSWER '35' FROM FILE SYNTHLINE

=> d ibib ed abs hitrn 1-16

L9   ANSWER 1 OF 35  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:        2006:513407  CAPLUS  Full-text
DOCUMENT NUMBER:         145:14738
TITLE:                   A combination of N-(3-methoxy-5-methylpyrazin-2-yl)-2-
                         (4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide
                         and an anti-mitotic agent for the treatment of cancer
INVENTOR(S):             Boyle, Francis Thomas; Curwen, John; Hughes, Andrew;
                         Johnstone, Donna
PATENT ASSIGNEE(S):      Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE:                  PCT Int. Appl., 23 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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     WO 2006056760        A1    20060601    WO 2005-GB4483          20051123
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
            KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
            MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
            SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
            VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       GB 2004-25854       A  20041125
ED   Entered STN:  01 Jun 2006
AB   A combination is disclosed comprising N-(3-methoxy-5-methylpyrazin-2-yl)-2-
     (4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide and an anti-mitotic
     cytotoxic agent.
IT   186497-07-4
     RL: PEP (Physical, engineering or chemical process); PYP (Physical
     process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (antitumor combination of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-
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        [1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide and an anti-mitotic
        agent)
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9   ANSWER 2 OF 35  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER:        2006:523875  CAPLUS  Full-text
DOCUMENT NUMBER:         145:159275
TITLE:                   ZD4054, a potent endothelin receptor A antagonist,
                         inhibits ovarian carcinoma cell proliferation
AUTHOR(S):               Rosano, Laura; Di Castro, Valeriana; Spinella,
                         Francesca; Decandia, Samantha; Natali, Pier Giorgio;
                         Bagnato, Anna
CORPORATE SOURCE:        Molecular Pathology and Ultrastructure Laboratory,
                         Regina Elena Cancer Institute, Rome, Italy
SOURCE:                  Experimental Biology and Medicine (Maywood, NJ, United
                         States) (2006), 231(6), 1132-1135
                         CODEN: EBMMBE; ISSN: 1535-3702
PUBLISHER:               Society for Experimental Biology and Medicine
DOCUMENT TYPE:           Journal
LANGUAGE:                English
ED   Entered STN:  05 Jun 2006
AB   Endothelin-1 (ET-1) is present at high concns. in ovarian cancer ascites and
     is overexpressed in primary and metastatic ovarian carcinomas.  In these
     tumors, the presence of ET-1 correlates with tumor grade, enhanced
     neovascularization, and with vascular endothelial growth factor (VEGF)
     expression.  ET-1 acts as an autocrine factor selectively through ETA receptor
     (ETAR), predominantly expressed in ovarian carcinoma cells resulting in
     increased VEGF production and VEGF-mediated angiogenic effects. Previous
     results demonstrated that in ovarian carcinoma cells, activation of the ET-
     1/ETAR axis promotes cell proliferation, neovascularization, and invasion,
     which are the principal hallmarks of tumor progression.  The present study was
     designed to investigate the in vitro effects of trans, trans-2(4-
     methoxydhenyl)-4-(1-3-benzodiazol-5-yl)-1- (dibutylaminocarbonylmethyl)-
     pyrrolidine-3-carboxylic acid (ZD4054), an orally active specific ETAR
     antagonist, on the ET-1-induced mitogenic effect in OVCA 433 and HEY ovarian
     carcinoma cell lines secreting ET-1 and expressing ETAR and ETBR mRNA.  We
     show that ETAR blockade by ZD4054 inhibits ET-1-induced mitogenic effects,
     while the ETBR antagonist, BQ 788, is ineffective.  In conclusion, our data
     demonstrate that ZD4054 is capable in inhibiting the proliferative activity of
     ET-1, indicating that this specific ETAR antagonist may be a potential
     candidate in developing novel treatment of ovarian carcinoma.
IT   186497-07-4, ZD4054
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (ZD4054 inhibits ovarian carcinoma cell proliferation)
REFERENCE COUNT:         17    THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9   ANSWER 3 OF 35  CAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER:        2005:1290072  CAPLUS  Full-text
DOCUMENT NUMBER:         144:46998
TITLE:                   The X-ray crystal structure of BRCA1 tandem BRCT
                         repeat and BACH1 phosphopeptide complex and methods
                         and compositions for antitumor drug design
INVENTOR(S):             Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac
                         A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.;
                         Smerdon, Stephen J.
PATENT ASSIGNEE(S):      Massachusetts Institute of Technology, USA
SOURCE:                  PCT Int. Appl., 360 pp.
```

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115454	A2	20051208	WO 2005-US15981	20050509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005247346	A1	20051208	AU 2005-247346	20050509
CA 2569003	A1	20051208	CA 2005-2569003	20050509
PRIORITY APPLN. INFO.:			US 2004-569131P P	20040507
			WO 2005-US15981 W	20050509

ED Entered STN: 09 Dec 2005
AB The present invention relates to compds. (e.g., peptidomimetics and non-peptides) that treat, prevent or stabilize cellular proliferative disorders and methods of treating, preventing, or stabilizing such disorders. The invention also provides three-dimensional structures of a BRCT domain-BACH1 phosphopeptide complex.
IT 186497-07-4, ZD-4054
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(X-ray crystal structure of BRCA1 tandem BRCT repeat and BACH1 phosphopeptide complex and methods and compns. for antitumor drug design)

L9 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2005:409543 CAPLUS Full-text
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005148535	A1	20050707	US 2004-975974	20041028
CA 2542904	A1	20050512	CA 2004-2542904	20041029
EP 1682565	A1	20060726	EP 2004-789809	20041029
R: DE, FR, GB				
PRIORITY APPLN. INFO.:			US 2003-516192P P	20031030
			WO 2004-CA1902 W	20041029

ED Entered STN: 13 May 2005
AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).
IT 186497-07-4, ZD-4054
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

L9 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2005:409357 CAPLUS Full-text
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005119217	A1	20050602	US 2004-975790		20041028
AU 2004284855	A1	20050512	AU 2004-284855		20041029
CA 2542884	A1	20050512	CA 2004-2542884		20041029
EP 1691842	A1	20060823	EP 2004-789807		20041029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004015779	A	20061226	BR 2004-15779		20041029
CN 1901939	A	20070124	CN 2004-80039601		20041029
NO 2006002420	A	20060731	NO 2006-2420		20060529
PRIORITY APPLN. INFO.:			US 2003-516263P	P	20031030
			WO 2004-CA1900	W	20041029

ED Entered STN: 13 May 2005

AB The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.

IT 186497-07-4, ZD-4054
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with chemotherapeutic agent)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2005:283298 CAPLUS Full-text
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916

WO 2005027842	A3	20051222			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004273910	A1	20050331	AU 2004-273910		20040916
CA 2538570	A1	20050331	CA 2004-2538570		20040916
EP 1670477	A2	20060621	EP 2004-788798		20040916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004014568	A	20061107	BR 2004-14568		20040916
CN 1878556	A	20061213	CN 2004-80033294		20040916
NO 2006001325	A	20060606	NO 2006-1325		20060323
PRIORITY APPLN. INFO.:			US 2003-504310P	P	20030918
			WO 2004-US30368	W	20040916

OTHER SOURCE(S): MARPAT 142:349042

ED Entered STN: 01 Apr 2005

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

IT 186497-07-4, ZD-4054
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorpromazine compound-antiproliferative drug antitumor combination)

L9 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 2005:232622 CAPLUS Full-text
DOCUMENT NUMBER: 142:303627
TITLE: Combination comprising n-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide and an LHRH analog and/or a bisphosphonate
INVENTOR(S): Gallagher, Neil
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023264	A1	20050317	WO 2004-GB3733	20040902

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004269956	A1	20050317	AU 2004-269956		20040902
CA 2537096	A1	20050317	CA 2004-2537096		20040902
EP 1663236	A1	20060607	EP 2004-768282		20040902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004013974	A	20061031	BR 2004-13974		20040902
CN 1878555	A	20061213	CN 2004-80032911		20040902
US 2006287241	A1	20061221	US 2006-569583		20060223
NO 2006001051	A	20060403	NO 2006-1051		20060303
PRIORITY APPLN. INFO.:			GB 2003-20806	A	20030905
			WO 2004-GB3733	W	20040902

ED Entered STN: 17 Mar 2005

AB A combination, comprising N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide, or a pharmaceutically acceptable salt thereof, and an LHRH analog and / or a bisphosphonate is described.

IT 186497-07-4
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antitumor combination comprising n-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide and an LHRH analog and/or a bisphosphonate)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 2005:508383 CAPLUS Full-text
DOCUMENT NUMBER: 143:318481
TITLE: Specific inhibition of the endothelin A receptor with ZD4054: clinical and pre-clinical evidence
AUTHOR(S): Morris, C. D.; Rose, A.; Curwen, J.; Hughes, A. M.; Wilson, D. J.; Webb, D. J.
CORPORATE SOURCE: Alderley Park, AstraZeneca, Cheshire, SK10 4TF, UK
SOURCE: British Journal of Cancer (2005), 92(12), 2148-2152
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 14 Jun 2005

AB Activation of the endothelin A receptor (ETA) by endothelin-1 (ET-1) mediates events that regulate mitogenesis, apoptosis, angiogenesis and metastasis in tumors. Specific blockade of ETA may have anticancer effects, while retaining beneficial endothelin B receptor (ETB)-mediated effects such as apoptosis and clearance of ET-1. ZD4054 is an orally active, specific ETA antagonist in clin. development. In receptor-binding studies, ZD4054 specifically bound to ETA with high affinity; no binding was detected at ETB. In a randomized placebo-controlled trial in eight healthy volunteers, a single oral dose of ZD4054 reduced forearm vasoconstriction in response to brachial artery infusion of ET-1, thus providing clin. evidence of ETA blockade. ETB blockade was assessed in an ascending, single-dose, placebo-controlled trial in 28 volunteers. For all doses of ZD4054, mean plasma ET-1 concns. measured at 4 and 24 h were within the placebo reference range (a rise in ET-1 would indicate ETB blockade) and there was no evidence of dose-related changes. These data confirm the specificity of ZD4054 for ETA, with no activity at ETB in a clin. or preclin. setting. As a result of this specificity, ZD4054 has the potential to block multiple ETA-induced pathol. processes, while allowing

beneficial ETB-mediated processes to continue, which may, in turn, lead to an effective cancer therapy.

IT 186497-07-4, ZD4054
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ZD4054 was potent antagonist of endothelin A receptor but not endothelin B receptor in human volunteer, pre-clin. receptor binding studies and may lead to effective cancer therapy)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2004:354796 CAPLUS Full-text
DOCUMENT NUMBER: 140:368653
TITLE: Endothelin receptor antagonist-EGF receptor tyrosine kinase inhibitor combination for the treatment of cancer
INVENTOR(S): Boyle, Francis Thomas; Curwen, Jon Owen; Gallagher, Neil James; Hancox, Ursula Joy; Hughes, Andrew Mark; Johnstone, Donna; Taylor, Sian Tomiko; Tonge, David William
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004035057	A1	20040429	WO 2003-GB4347		20031007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2501959	A1	20040429	CA 2003-2501959		20031007
AU 2003269259	A1	20040504	AU 2003-269259		20031007
EP 1553950	A1	20050720	EP 2003-751038		20031007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003015140	A	20050816	BR 2003-15140		20031007
CN 1703224	A	20051130	CN 2003-80101310		20031007
JP 2006510605	T	20060330	JP 2004-544431		20031007
NO 2005001658	A	20050506	NO 2005-1658		20050404
ZA 2005002874	A	20060222	ZA 2005-2874		20050408
US 2006122180	A1	20060608	US 2005-530794		20050408
PRIORITY APPLN. INFO.:			GB 2002-23854	A	20021012
			WO 2003-GB4347	W	20031007

ED Entered STN: 30 Apr 2004

AB A combination, comprising an endothelin receptor antagonist (e.g. ZD4054), or a pharmaceutically acceptable salt thereof, and an EGF receptor tyrosine kinase inhibitor (e.g. ZD1839), or a pharmaceutically acceptable salt thereof,

is described. The combination of the invention is useful for the treatment of cancer, e.g. prostate cancer.

IT 186497-07-4, ZD 4054
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endothelin receptor antagonist-EGF receptor tyrosine kinase inhibitor combination for treatment of cancer)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2004:331974 CAPLUS Full-text
DOCUMENT NUMBER: 140:332519
TITLE: 5-HT1B/1D receptor agonists for the treatment of headache resulting from administering an endothelin receptor antagonist
INVENTOR(S): Curwen, Jon Owen; Hughes, Andrew Mark; Johnstone, Donna; Morris, Clive Dylan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032922	A1	20040422	WO 2003-GB4338	20031006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003274307	A1	20040504	AU 2003-274307	20031006
EP 1551395	A1	20050713	EP 2003-758297	20031006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006508933	T	20060316	JP 2004-542622	20031006
US 2006009512	A1	20060112	US 2005-530232	20050404
PRIORITY APPLN. INFO.:			GB 2002-23367 A	20021009
			WO 2003-GB4338 W	20031006

ED Entered STN: 23 Apr 2004
AB The invention discloses the use of a 5-HT1B/1D receptor agonist in the treatment or prevention of headache that results from administering an endothelin receptor antagonist. The invention also discloses a combination comprising an endothelin receptor antagonist and a 5-HT1B/1D receptor agonist.
IT 186497-07-4, ZD 4054
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT1B/1D receptor agonists for the treatment of headache resulting from administering an endothelin receptor antagonist)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2004:182737 CAPLUS Full-text
DOCUMENT NUMBER: 140:210754
TITLE: Therapeutic use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide
INVENTOR(S): Tonge, David William; Taylor, Sian Tomiko; Boyle, Francis Thomas; Hughes, Andrew Mark; Johnstone, Donna; Ashford, Marianne Bernice; Barrass, Nigel Charles
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018044	A2	20040304	WO 2003-GB3653	20030820
WO 2004018044	A3	20040506		
WO 2004018044	A8	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2496476	A1	20040304	CA 2003-2496476	20030820
AU 2003255835	A1	20040311	AU 2003-255835	20030820
BR 2003013655	A	20050621	BR 2003-13655	20030820
EP 1545710	A2	20050629	EP 2003-792501	20030820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1688365	A	20051026	CN 2003-824409	20030820
JP 2004083590	A	20040318	JP 2003-299605	20030825
JP 3663202	B2	20050622		
JP 2005097312	A	20050414	JP 2004-311829	20041027
NO 2005000689	A	20050321	NO 2005-689	20050209
US 2006094729	A1	20060504	US 2005-524963	20050218
PRIORITY APPLN. INFO.:			GB 2002-19660 A	20020823
			WO 2003-GB3653 W	20030820
			JP 2003-299605 A3	20030825

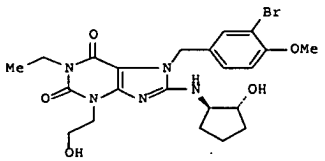
ED Entered STN: 05 Mar 2004
AB The use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide, or a pharmaceutically acceptable salt thereof, in the treatment of cancer and/or pain in a warm blooded animal such as man is described.
IT 186497-07-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide)

L9 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1036580 CAPLUS Full-text

DOCUMENT NUMBER: 145:389433
TITLE: PDE 5 inhibitors for treatment of benign prostatic hyperplasia or lower urinary tract symptoms
INVENTOR(S): Pickett, Cecil; Cuffie-Jackson, Cynthia
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 73pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006104870	A2	20061005	WO 2006-US10715	20060323
WO 2006104870	A3	20061228		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007004745	A1	20070104	US 2006-387280	20060323

PRIORITY APPLN. INFO.: US 2005-665348P P 20050325
OTHER SOURCE(S): MARPAT 145:389433
ED Entered STN: 05 Oct 2006
GI



I

AB The use of PDE 5 inhibitors in methods for the treatment of benign prostatic hyperplasia or lower urinary tract symptoms and other physiol. disorders, as a monotherapy and in combination with other active agents is disclosed. For example, a representative compound useful in the methods of the invention formula (I).

IT 186497-07-4, ZD-4054
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDE 5 inhibitors for treatment of benign prostatic hyperplasia or lower urinary tract symptoms)

L9 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:495877 CAPLUS Full-text
DOCUMENT NUMBER: 144:481050
TITLE: Methods of using Phosphodiesterase-V inhibitors for the treatment of congestive heart failure
INVENTOR(S): Cuffie-Jackson, Cynthia; Veltri, Enrico P.
PATENT ASSIGNEE(S): Schering Corp., USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006055573	A2	20060526	WO 2005-US41386	20051116
WO 2006055573	A3	20060921		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2004-629030P P 20041118
OTHER SOURCE(S): MARPAT 144:481050
ED Entered STN: 26 May 2006

AB The use of Phosphodiesterase-V (PDE-V) inhibitors for the treatment of congestive heart failure and other physiol. disorders, as a monotherapy and in combination with other active agents are disclosed.

IT 186497-07-4, ZD-4054
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDE5 inhibitors for treatment of congestive heart failure)

L9 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:800517 CAPLUS Full-text
DOCUMENT NUMBER: 142:166029
TITLE: N-(3-Methoxy-5-methylpyrazin-2-yl)-2-[4-(1,3,4-oxadiazol-2-yl)phenyl]pyridine-3-sulfonamide (ZD4054 Form 1)
AUTHOR(S): Stensland, Birgitta; Roberts, Ron J.
CORPORATE SOURCE: Preformulation and Biopharmaceutics, Solid State Analysis and Physical Chemistry, AstraZeneca PAR&D/SBBG B341:3, Soedertaelje, SE-151 85, Swed.
SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2004), E60(10), o1817-o1819
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/graphics/htmlborder.gif
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

ED Entered STN: 01 Oct 2004
AB The title compound, C19H16N6O4S, crystallizes from N-methylpyridine in the centrosym. space group P21/n with Z = 4. Crystallog. data are given. The mol. has 11 heteroatoms, of which only one is protonated. This potential H-bond donor, viz. the NH amide group, participates in both intra- and intermol. H-bond interactions, thus contributing to the stabilization of the mol. conformation and the linking of mols. as dimers. The hairpin-like folded mol. is arranged with three of its four aromatic rings in two parallel planes intersected by a sulfonamide moiety. In this way, the mols. stack efficiently, facilitated by short-range van der Waals forces. No residual volume for solvent inclusion was found.
IT 186497-07-4, ZD4054
RL: PRP (Properties)
(crystal structure of)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:132770 CAPLUS Full-text
DOCUMENT NUMBER: 126:144291
TITLE: N-pyrazinyl-2-phenyl-3-pyridinesulfonamides and analogs endothelin receptor antagonists
INVENTOR(S): Bradbury, Robert Hugh; Butlin, Roger John; James, Roger
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

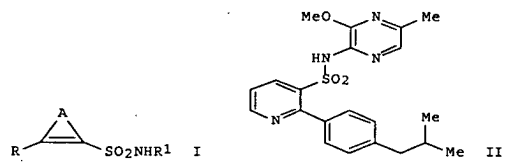
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640681	A1	19961219	WO 1996-GB1295	19960603
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2219742	A1	19961219	CA 1996-2219742	19960603
CA 2219742	C	20070116		
AU 9658403	A	19961230	AU 1996-58403	19960603
AU 715041	B2	20000113		
EP 832082	A1	19980401	EP 1996-919941	19960603
EP 832082	B1	20011121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1192739	A	19980909	CN 1996-196149	19960603
CN 1097051	B	20021225		
BR 9608611	A	19990511	BR 1996-8611	19960603
JP 11509175	T	19990817	JP 1997-500209	19960603
JP 3193058	B2	20010730		
HU 9802300	A2	19991028	HU 1998-2300	19960603
NZ 308619	A	20000128	NZ 1996-308619	19960603
RU 2172738	C2	20010827	RU 1998-100054	19960603
AT 209200	T	20011215	AT 1996-919941	19960603
SK 282338	B6	20020107	SK 1997-1680	19960603
CZ 289387	B6	20020116	CZ 1997-3887	19960603

PT 832082	T	20020429	PT 1996-919941	19960603
IL 122464	A	20020523	IL 1996-122464	19960603
ES 2168487	T3	20020616	ES 1996-919941	19960603
PL 187897	B1	20041029	PL 1996-324660	19960603
ZA 9604615	A	19961209	ZA 1996-4615	19960604
US 5866568	A	19990202	US 1996-658969	19960604
HR 960272	B1	20060630	HR 1996-272	19960606
NO 9705700	A	19971205	NO 1997-5700	19971205
NO 314503	B1	20030331		
HK 1005801	A1	20021220	HK 1998-105010	19980606
US 6060475	A	20000509	US 1998-211483	19981214
US 6258817	B1	20010710	US 2000-504364	20000215

PRIORITY APPLN. INFO.:

GB 1995-11507	A	19950607
GB 1995-19666	A	19950927
WO 1996-GB1295	W	19960603
US 1996-658969	A3	19960604
US 1998-211483	A3	19981214

OTHER SOURCE(S): MARPAT 126:144291
ED Entered STN: 28 Feb 1997
GI



I II

AB Title compds. [I; A = atoms to complete an (un)substituted pyridine ring; R = (un)substituted Ph; R1 = (un)substituted heteroarom. ring containing 2 N atoms] were prepared Thus, iso-Bu N-(3-methoxy-5-methyl-2-pyrazinyl)carbamate was amidated by 2-chloropyridine-3-sulfonyl chloride (preparation each given) and the product arylated by 4-(Me2CHCH2)C6H4B(OH)2 to give, after deprotection, title compound II. Data for biol activity of I were given.
IT 186497-07-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of n-pyrazinyl-2-phenyl-3-pyridinesulfonamides and analogs endothelin receptor antagonists)

L9 ANSWER 16 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2007:5546 USPATFULL Full-text
TITLE: Methods of treating benign prostatic hyperplasia or lower urinary tract symptoms by using PDE 5 inhibitors
INVENTOR(S): Pickett, Cecil, Far Hills, NJ, UNITED STATES
Cuffie-Jackson, Cynthia, Far Hills, NJ, UNITED STATES
PATENT ASSIGNEE(S): Schering-Plough Corporation (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2007004745	A1	20070104

APPLICATION INFO.: US 2006-387280 A1 20060323 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-665348P	20050325 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530, US
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 863
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of PDE 5 inhibitors in methods for the treatment of benign prostatic hyperplasia or lower urinary tract symptoms and other physiological disorders, as a monotherapy and in combination with other active agents is disclosed. For example, a representative compound useful in the methods of the invention is: ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4, ZD-4054
(PDE 5 inhibitors for treatment of benign prostatic hyperplasia or lower urinary tract symptoms)

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L9 ANSWER 17 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2006:334626 USPATFULL Full-text
TITLE: Combination comprising N-(3-methoxy-5-methylpyrazin-2yl)-2-(4-[1,3,4-oxadiazol-2-yl]pyridine-3-sulphonamide and an lhrh analogue and/or bisphosphonate
INVENTOR(S): Gallagher, Neil, Cambridge, UNITED KINGDOM
PATENT ASSIGNEE(S): AstraZeneca AB, Sodertalje, SWEDEN, 151 85 (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006287241	A1	20061221	
APPLICATION INFO.:	US 2004-569583	A1	20040902	(10)
	WO 2004-GB3733		20040902	
			20060223	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2003-20806	20030905

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ASTRAZENECA R&D BOSTON, 35 GATEHOUSE DRIVE, WALTHAM, MA, 02451-1215, US
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
LINE COUNT: 745
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A combination, comprising N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide, or a pharmaceutically

acceptable salt thereof, and an LHRH analogue and/or a bisphosphonate is described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4
(antitumor combination comprising n-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide and an LHRH analog and/or a bisphosphonate)

L9 ANSWER 18 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2006:144662 USPATFULL Full-text
TITLE: Therapeutic treatment
INVENTOR(S): Boyle, Francis Thomas, Cheshire, UNITED KINGDOM
Curwen, Jon Owen, Cheshire, UNITED KINGDOM
Gallagher, Neil James, Cheshire, UNITED KINGDOM
Hancox, Ursula Joy, Cheshire, UNITED KINGDOM
Hughes, Andrew Mark, Cheshire, UNITED KINGDOM
Johnstone, Donna, Cheshire, UNITED KINGDOM
Taylor, Sian Tomiko, Cheshire, UNITED KINGDOM
Tonge, David William, Cheshire, UNITED KINGDOM

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006122180	A1	20060608	
APPLICATION INFO.:	US 2003-530794	A1	20031007	(10)
	WO 2003-GB4347		20031007	
			20050408	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2002-23854	20021012

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ASTRAZENECA R&D BOSTON, 35 GATEHOUSE DRIVE, WALTHAM, MA, 02451-1215, US
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 735
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A combination, comprising an endothelin receptor antagonist, or a pharmaceutically acceptable salt thereof, and an EGFR TKI, or a pharmaceutically acceptable salt thereof is described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4, ZD 4054
(endothelin receptor antagonist-EGF receptor tyrosine kinase inhibitor combination for treatment of cancer)

L9 ANSWER 19 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2006:111781 USPATFULL Full-text
TITLE: N-(-3-methoxy-5-methylpyrazin-2-yl)-2-(4-'1,3,4-oxadiazol-2-yl!phenyl)pyridine-3 sulphonamide as an anticancer agent
INVENTOR(S): Tonge, David William, Macclesfield, UNITED KINGDOM
Tayer, Sian Tomiko, Macclesfield, UNITED KINGDOM
Boyle, Francis Thomas, Macclesfield, UNITED KINGDOM
Hughes, Andrew Mark, Macclesfield, UNITED KINGDOM

Johnstone, Donna, Macclesfield, UNITED KINGDOM
Ashford, Marianne Bernice, Macclesfield, UNITED KINGDOM
Barrass, Nigel Charles, Macclesfield, UNITED KINGDOM
PATENT ASSIGNEE(S): AStraZeneca AB, Sodertalje, SWEDEN, SE-151 85 (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006094729	A1	20060504	
APPLICATION INFO.:	US 2003-524963	A1	20030820	(10)
	WO 2003-GB3653		20030820	
			20050218	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2002-19660	20020823

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ASTRAZENECA R&D BOSTON, 35 GATEHOUSE DRIVE, WALTHAM, MA, 02451-1215, US
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1-25
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide, or a pharmaceutically acceptable salt thereof, in the treatment of cancer and/or pain in a warm blooded animal such as man is described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4
(therapeutic use of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulfonamide)

L9 ANSWER 20 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2006:10658 USPATFULL Full-text
TITLE: 5-ht 1b/1d receptor agonists for the treatment of headache resulting from administering an endothelin receptor antagonist
INVENTOR(S): Curwen, Jon Owen, Macclesfield, UNITED KINGDOM
Hughes, Andrew Mark, Macclesfield, UNITED KINGDOM
Johnstone, Donna, Macclesfield, UNITED KINGDOM
Morris, Clive Dylan, Macclesfield, UNITED KINGDOM
PATENT ASSIGNEE(S): AstraZeneca AB, Sodertalje, SWEDEN, SE-151 85 (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006009512	A1	20060112	
APPLICATION INFO.:	US 2003-530232	A1	20031006	(10)
	WO 2003-GB4338		20031006	
			20050404	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2002-23367	20021009

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: ASTRAZENECA R&D BOSTON, 35 GATEHOUSE DRIVE, WALTHAM, MA, 02451-1215, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1-7
LINE COUNT: 859
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of a 5-HT.sub.1B/1D receptor agonist in the treatment or prevention of headache that results from administering an endothelin receptor antagonist; and the combination, comprising an endothelin receptor antagonist and a 5-HT.sub.1B/1D receptor agonist is described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4, ZD 4054
(5-HT1B/1D receptor agonists for the treatment of headache resulting from administering an endothelin receptor antagonist)

L9 ANSWER 21 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2005:171786 USPATFULL Full-text
TITLE: IAP nucleobase oligomers and oligomeric complexes and uses thereof
INVENTOR(S): LaCasse, Eric, Ottawa, CANADA
McManus, Daniel, Ottawa, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005148535	A1	20050707	
APPLICATION INFO.:	US 2004-975974	A1	20041028	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-516192P	20031030 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110, US
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 3022
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides nucleobase oligomers and oligomer complexes that inhibit expression of an IAP polypeptide, and methods for using them to induce apoptosis in a cell. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compositions. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4, ZD-4054
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

L9 ANSWER 22 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2005:138567 USPATFULL Full-text
TITLE: Methods and reagents for the treatment of proliferative diseases

INVENTOR(S): LaCasse, Eric, Ottawa, CANADA
McManus, Daniel, Ottawa, CANADA
Durkin, Jon P., Montreal, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005119217	A1	20050602
APPLICATION INFO.:	US 2004-975790	A1	20041028 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-516263P	20031030 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110, US
NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 5896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention features methods, compositions, and kits for treating a patient having a proliferative disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4, ZD-4054
(sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent)

L9 ANSWER 23 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2001:107899 USPATFULL Full-text
TITLE: Substituted pyrazin-2-yl-sulphonamide (-3-pyridyl) compounds and uses thereof
INVENTOR(S): Bradbury, Robert Hugh, Wilmslow, United Kingdom
Butlin, Roger John, Macclesfield, United Kingdom
James, Roger, Congleton, United Kingdom
PATENT ASSIGNEE(S): Zeneca Ltd., United Kingdom (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6258817	B1	20010710
APPLICATION INFO.:	US 2000-504364		20000215 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1998-211483, filed on 14 Dec 1998, now patented, Pat. No. US 6060475 Division of Ser. No. US 1996-658969, filed on 4 Jun 1996, now patented, Pat. No. US 5866568		

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1995-11507	19950607
	GB 1995-19666	19950927

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Truong, Tamthom N.
LEGAL REPRESENTATIVE: Mitchell, Kenneth F.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1

LINE COUNT: 3591
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful compounds of the formula I, in which A.sup.1, A.sup.2, A.sup.3, A.sup.4, B.sup.1, m, Ar, W, X, Y, Z and R.sup.1 have any of the meanings defined herein, and their pharmaceutically acceptable salts, and pharmaceutical compositions containing them. The novel compounds possess endothelin receptor antagonist activity and are useful, for example, in the treatment of diseases or medical conditions in which elevated or abnormal levels of endothelin play a significant causative role. The invention further concerns processes for the manufacture of the novel compounds and the use of the compounds in medical treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4P
(preparation of n-pyrazinyl-2-phenyl-3-pyridinesulfonamides and analogs endothelin receptor antagonists)

L9 ANSWER 24 OF 35 USPATFULL on STN
ACCESSION NUMBER: 2000:57769 USPATFULL Full-text
TITLE: Substituted pyrazin-2-yl-sulphonamide-(3-pyridyl) compounds and uses thereof
INVENTOR(S): Bradbury, Robert Hugh, Wilmslow, United Kingdom
Butlin, Roger John, Macclesfield, United Kingdom
James, Roger, Congleton, United Kingdom
PATENT ASSIGNEE(S): Zeneca Limited, United Kingdom (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6060475		20000509
APPLICATION INFO.:	US 1998-211483		19981214 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-658969, filed on 4 Jun 1996, now patented, Pat. No. US 5866568		

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1995-11507	19950607
	GB 1995-19666	19950927

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
ASSISTANT EXAMINER: Truong, Tamthom N.
LEGAL REPRESENTATIVE: Mitchell, Kenneth F.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 3622
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful compounds of the formula I, in which A.sup.1, A.sup.2, A.sup.3, A.sup.4, B.sup.1, m, Ar, W, X, Y, Z and R.sup.1 have any of the meanings defined herein, and their pharmaceutically acceptable salts, and pharmaceutical compositions containing them. The novel compounds possess endothelin receptor antagonist activity and are useful, for example, in the treatment of diseases or medical conditions in which elevated or abnormal levels of endothelin play a significant causative role. The invention further concerns processes for the manufacture of the novel compounds and the use of the compounds in medical treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4P

(preparation of n-pyrazinyl-2-phenyl-3-pyridinesulfonamides and analogs endothelin receptor antagonists)

L9 ANSWER 25 OF 35 USPATFULL on STN
ACCESSION NUMBER: 1999:15922 USPATFULL Full-text
TITLE: Heterocyclic compounds
INVENTOR(S): Bradbury, Robert Hugh, Cheshire, United Kingdom
Butlin, Roger John, Cheshire, United Kingdom
James, Roger, Cheshire, United Kingdom
PATENT ASSIGNEE(S): Zeneca Limited, London, United Kingdom (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5866568		19990202	
APPLICATION INFO.:	US 1996-658969		19960604	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1995-11507	19950607
	GB 1995-19666	19950927

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Ngo, Tamthom T.
LEGAL REPRESENTATIVE: Elder, Richard A.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 3631
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful compounds of the formula I, in which A.sup.1, A.sup.2, A.sup.3, A.sup.4, B.sup.1, m, Ar, W, X, Y, Z and R.sup.1 have any of the meanings defined herein, and their pharmaceutically acceptable salts, and pharmaceutical compositions containing them. The novel compounds possess endothelin receptor antagonist activity and are useful, for example, in the treatment of diseases or medical conditions in which elevated or abnormal levels of endothelin play a significant causative role. The invention further concerns processes for the manufacture of the novel compounds and the use of the compounds in medical treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 186497-07-4P
(preparation of n-pyrazinyl-2-phenyl-3-pyridinesulfonamides and analogs endothelin receptor antagonists)

L9 ANSWER 26 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 2007:502 IMSDRUGNEWS
TITLE: zibotentan AstraZeneca phase change I, Japan (prostate cancer)
SOURCE: R&D Focus Drug News (29 Jan 2007).
WORD COUNT: 37
TEXT:

AstraZeneca is conducting a phase I trial of zibotentan(ZD 4054) in Japan for the treatment of prostate cancer. The agent, a selective endothelin A receptor

antagonist, is also undergoing phase II evaluation in Europe for this indication.

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: Phase I. Japan

L9 ANSWER 27 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 2005:3412 IMSDRUGNEWS
TITLE: zibotentan AstraZeneca clinical data (phase II) (prostate cancer)
SOURCE: R&D Focus Drug News (30 May 2005).
WORD COUNT: 142
TEXT:

AstraZeneca's AZD 4054, a selective endothelin A receptor antagonist, is undergoing phase II evaluation as a therapy for prostate cancer. Preliminary results from an open-label, multicenter phase IIa trial were presented at the 41st Annual Meeting of the American Society of Clinical Oncology, 13-17 May 2005, Orlando, USA. During this dose-escalation study, AZD 4054 was administered orally to 16 patients with hormone refractory prostate cancer. Results showed that the agent was well tolerated, and dose limiting toxicities, which included grade 3 dyspnea and peripheral edema, were observed at 22.5 mg. The maximum tolerated dose was identified as 15 mg; patients receiving this dose reported side effects such as headache, peripheral edema, fatigue, nasal congestion and nausea, however, no dose-limiting toxicities were observed at this dose. An average hemoglobin decrease of 0.8 g/dL was observed and the average weight change was 0.7 kg.

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: clinical data (phase II).

L9 ANSWER 28 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 2005:2912 IMSDRUGNEWS
TITLE: zibotentan AstraZeneca clinical data (phase I)
SOURCE: R&D Focus Drug News (9 May 2005).
WORD COUNT: 223
TEXT:

At the 96th Annual Meeting of the American Association for Cancer Research, 16-20 April 2005, Anaheim, USA, AstraZeneca presented further preclinical data for AZD 4054 (ZD 4054), a selective endothelin A receptor antagonist, under evaluation for the potential treatment of solid tumors including prostate cancer. In vitro, AZD 4054 was demonstrated to block endothelin A receptor (ETA) mediated activation of p44/42 MAPK in murine osteoblast and human immature pre-osteoblast cells in response to endothelin-1 (ET-1) treatment and also inhibited ETA-mediated proliferation of the human immature pre-osteoblast cells in response to ET-1. Additionally, in both in vitro and in vivo models of ovarian carcinoma AZD 4054 demonstrated antitumor activity as a monotherapy and as a combination therapy with paclitaxel.

AstraZeneca also presented data from a single dose, double-blind, phase I study, designed to demonstrate the ability of AZD 4054 to specifically inhibit endothelin-1 (ET-1) activity through the endothelin A receptor (ETA) in vivo, in which 8 healthy male volunteers were randomized to receive either 30 mg or 10 mg AZD 4054 doses or placebo. Results demonstrated that AZD 4054 specifically inhibited ETA in humans.

A spokesperson for AstraZeneca informed R&D focus that a phase II trial of AZD 4054 is ongoing in Europe in the treatment of hormone refractory prostate cancer and that further trials of the agent are planned in the treatment of other cancers.

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: clinical data (phase I).

L9 ANSWER 29 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 2003:3505 IMSDRUGNEWS
TITLE: zibotentan AstraZeneca phase change II, Europe (cancer)
SOURCE: R&D Focus Drug News (4 Aug 2003).
WORD COUNT: 54
TEXT:

AZD 4054, a selective endothelin A receptor antagonist, is being evaluated in phase II trials in Europe as a potential treatment of solid tumors. This was announced at AstraZeneca's Second Quarter and Half Year Results 2003 meeting, 24 July 2003, London, UK. The company expects regulatory submissions in the USA and Europe post 2005.

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: Phase II. Europe
STATUS: new phase

L9 ANSWER 30 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 2002:3713 IMSDRUGNEWS
TITLE: zibotentan AstraZeneca phase change I, Europe (cancer)
SOURCE: R&D Focus Drug News (18 Nov 2002).
WORD COUNT: 87
TEXT:

AstraZeneca is developing an endothelin A receptor antagonist, ZD 4054, for the treatment of solid tumors, including prostate cancer. It was announced at the company's Annual Business Review, 7 November 2002, London, UK, that phase I evaluation has completed and phase II trials in prostate cancer patients are scheduled to commence by end 2002.

ZD 4054 binds specifically and reversibly to the endothelin A receptor, with no demonstrable binding to the endothelin B receptor. The agent has oral bioavailability and was well tolerated in a phase I trial.

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: Phase I. Europe
STATUS: new phase

L9 ANSWER 31 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 2000:3 IMSDRUGNEWS
TITLE: ZD 1611, zibotentan AstraZeneca discontinued, UK
SOURCE: R&D Focus Drug News (10 Jan 2000).
WORD COUNT: 31
TEXT:

AstraZeneca's endothelin A antagonists, ZD 1611 and ZD 4054, have been discontinued from further development. These compounds were undergoing preclinical studies in the UK for the potential treatment of heart failure.

CHEMICAL NAME: ZD 1611
CLASSIFICATION: C1D Coronary Therapy
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: discontinued. United Kingdom

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: AstraZeneca
DEVELOPMENT STATUS: discontinued. United Kingdom

L9 ANSWER 32 OF 35 IMSDRUGNEWS COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 1998:1064 IMSDRUGNEWS
TITLE: zibotentan Zeneca endothelin antagonist for heart failure
SOURCE: R&D Focus Drug News (23 Mar 1998).
WORD COUNT: 21
TEXT:

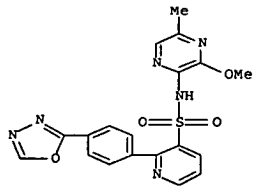
Zeneca is developing the endothelin antagonist ZD 4054 in preclinical trials in the UK as a potential therapy for heart failure.

CHEMICAL NAME: zibotentan; AZD 4054; ZD 4054
CAS REGISTRY NUMBER: 186497-07-4
CLASSIFICATION: L1X9 All Other Antineoplastics
COMPANY NAME: Zeneca
STATUS: new drug

L9 ANSWER 33 OF 35 IMSRESEARCH COPYRIGHT 2007 IMSWORLD on STN

ACCESSION NUMBER: 1998:326 IMSRESEARCH
SOURCE: R&D Focus, (29 Jan 2007)
GENERIC NAME: zibotentan
REFERENCE: pINN
LABORATORY NAME: AZD 4054; ZD 4054
CHEMICAL NAME: N-(3-methoxy-5-methylpyrazinyl)-2-[4-(1,3,4-oxadiazol-2-yl)phenyl]- 3-pyridinesulfonamide
CAS REGISTRY NO.: 186497-07-4

STRUCTURE:



DERIVATIVE(S): 186497-07-4ZD 4054
CLASSIFICATION: L1X9 All Other Antineoplastics
INDICATION: cancer; solid tumor; prostate cancer
ACTION: endothelin antagonist
HIGHEST DEV. PHASE: Phase II (40)
LATEST INFORMATION: AstraZeneca is conducting a phase I trial of zibotentan(ZD 4054) in Japan for the treatment of prostate cancer. The agent, a selective endothelin A receptor antagonist, is also undergoing phase II evaluation in Europe for this indication.

CURRENT DEVELOPMENT STATUS:

Type	Status	Stage	Region	Indication
Highest Phase	Phase II	40		
Phase	Phase II		Europe	prostate cancer
Phase	Preclinical		Europe	solid tumor
Phase	Discontinued		United Kingdom	heart failure
Phase	Phase I		Japan	prostate cancer

COMPANY INFORMATION:

Type	Company	Nationality
Originator	AstraZeneca	United Kingdom
Assignee	Zeneca	

PATENT SUMMARY:
Product: WO 96/40681 1996, priority UK 11507 1995, designating 82 states.

COMMERCIAL SUMMARY:
AstraZeneca is developing zibotentan, a selective endothelin A receptor antagonist, for the treatment of solid tumors including prostate cancer and ovarian cancer. Phase II trials of zibotentan in the treatment of patients with

hormone refractory prostate cancer are under way in Europe. Preclinical studies in a wide range of cancers, including ovarian cancer, are ongoing in Europe. Zibotentan had been previously investigated as a potential therapy for heart failure but development for this indication was discontinued in December 1999. In June 1995 AstraZeneca filed a priority patent application in the UK. Phase II trials of zibotentan are under way in Europe (AstraZeneca, JUL 2003). This ongoing phase II trial is evaluating zibotentan in the treatment of patients with hormone refractory prostate cancer and further clinical trials are planned to assess zibotentan in the treatment of other cancer indications (AstraZeneca, APR 2005). Preliminary results from this trial have been reported (AstraZeneca, MAY 2005). Results from this trial will determine the progression into phase III and will complete by end of third quarter 2006 (AstraZeneca, JUN 2006). Phase I evaluation has completed and results reported (AstraZeneca, NOV 2002). Further phase I results have been reported (AstraZeneca, APR 2005). A phase I trial is under way in Japan for the treatment of prostate cancer (Pharma Japan, DEC 2006). Preclinical studies in a wide range of cancers, including ovarian cancer and prostate cancer, are ongoing in Europe (AstraZeneca, APR 2005). Zibotentan had been previously investigated as potential therapy for heart failure but development for this indication was discontinued (AstraZeneca, DEC 1999). AstraZeneca, confirmed phase II for solid tumor, OCT 2003. AstraZeneca reported phase II ongoing in Europe, solid tumors, JAN 2004; OCT 2004; JAN 2005. AstraZeneca expects a phase II trial of zibotentan in patients with hormone refractory prostate cancer to be completed by third quarter 2006 (AstraZeneca, JUN 2006). Regulatory filings for zibotentan are anticipated in EU and USA post 2007 for the treatment of solid tumors (AstraZeneca, OCT 2004). AstraZeneca expected regulatory submissions to be filed in the USA and Europe post 2006 (AstraZeneca, JAN 2004). Latest prediction Analyst, Bear Stearns, reporting on AstraZeneca, predicts a launch for AZD 4054 in 2007 for the treatment of metastatic hormone refractory prostate cancer; estimates sales of US$10 million in 2007, US$30 million in 2008, US$50 million in 2009 and US$60 million in 2010 (Bear Stearns, JUN 2005). >Bear Stearns Analyst, Bear Stearns, reporting on AstraZeneca, estimates sales for AZD 4054 of US$10 million in 2006 and US$30 million in 2008 (Bear Stearns, JAN 2004). Credit Suisse First Boston Analyst, Credit Suisse First Boston, reporting on AstraZeneca, estimates sales for AZD 4054 of US$4 million in 2008 and US$50 million in 2009 (Credit Suisse First Boston, MAY 2005). Deutsche Bank> >Analyst, Deutsche Bank, reporting on AstraZeneca, predicts the commencement of a phase III study with AZD 4054 in 2005 (Deutsche Bank, OCT 2004) Morgan Stanley Analyst, Morgan Stanley, reporting on AstraZeneca, estimates sales for AZD 4054 of US$23 million in 2008, US$158 million in 2010 and peak sales of US$1 billion (Morgan Stanley, OCT 2004).

SCIENTIFIC SUMMARY:
Zibotentan specifically and reversibly binds to the endothelin A receptor, and showed a 10000-fold greater affinity for the endothelin A receptor than the endothelin B receptor. The agent demonstrated oral bioavailability. In preclinical studies, zibotentan blocked endothelin A receptor (ETA) mediated activation of p44/42 MAPK in murine osteoblast and human immature pre-osteoblast cells in response to endothelin-1 (ET-1) treatment. In response to ET-1 treatment, zibotentan also inhibited ETA-mediated proliferation of the human immature pre-osteoblast cells (96th AACR, Abs 1512, APR 2005). Additionally, in both in vitro and in vivo models of ovarian carcinoma zibotentan demonstrated antitumor activity as a monotherapy and as a combination therapy with paclitaxel. In vitro, 1 mcM zibotentan inhibited cell proliferation and reduced VEGF secretion by 35%. It also enhanced paclitaxel-induced apoptosis in HEY and OVCA 433 ovarian carcinoma cell lines. In vivo, zibotentan monotherapy inhibited HEY xenograft growth at doses ranging from 10-50 mg/kg/day ip administered for three weeks. Zibotentan administered at 25 mg/kg/day for 21 days reduced tumor growth by 65% compared with control, a comparable tumor reduction to that observed following paclitaxel treatment.

Furthermore, zibotentan administered in combination with paclitaxel resulted in enhanced paclitaxel activity and led to partial or complete tumor regression (96th AACR, Abs 5830, APR 2005). Results of a phase I trial in healthy volunteers demonstrated that zibotentan was well tolerated and confirmed specificity of the agent (AstraZeneca, NOV 2002). In a single dose, double-blind, phase I study, designed to demonstrate the ability of zibotentan to specifically inhibit endothelin-1 (ET-1) activity through the endothelin A receptor (ETA) in vivo, eight healthy male volunteers, were randomized to receive either 30 mg or 10 mg zibotentan doses or placebo. The study used forearm vasoconstriction as a measure of zibotentan activity in response to ET-1 (a known vasoconstrictor) brachial artery infusion. Results demonstrated that zibotentan specifically inhibited ETA in humans (96th AACR, Abs 4187, APR 2005). In an open-label, multicenter, dose-escalation phase IIa trial, zibotentan was administered orally to 16 patients with hormone refractory prostate cancer. Results showed that the agent was well tolerated, and dose limiting toxicities, which included grade 3 dyspnea and peripheral edema, were observed at 22.5 mg. The maximum tolerated dose was identified as 15 mg; patients receiving this dose reported side effects such as headache, peripheral edema, fatigue, nasal congestion and nausea, however, no dose-limiting toxicities were observed at this dose. An average hemoglobin decrease of 0.8 g/dL was observed and the average weight change was 0.7 kg (41st ASCO, Abs 4628, MAY 2005).

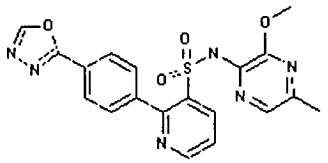
DEVELOPMENT HISTORY:

2006	Phase I, Japan (prostate cancer).
JUL 2003	Phase II, Europe (prostate cancer).
MAY 2002	Phase I, Europe (cancer).
DEC 1999	Discontinued (heart failure).
APR 1999	Astra/Zeneca merger.
MAR 1998	Preclinical, UK.
JUN 1995	Priority product patent application filed in the UK, by Zeneca.

L9 ANSWER 34 OF 35 PROUSDDR COPYRIGHT 2007 PROUS SCIENCE on STN

ACCESSION NUMBER:	2003:6 PROUSDDR Full-text
DOCUMENT NUMBER:	258506
CHEMICAL NAME:	N-(3-Methoxy-5-methylpyrazin-2-yl)-2-(4-(1,3,4-oxadiazol-2-yl)phenyl)pyridine-3-sulfonamide
DRUG NAME:	ZD-4054
GENERIC NAME:	Zibotentan (Rec INN)
CAS REGISTRY NUMBER:	186497-07-4
MOLECULAR FORMULA:	C19 H16 N6 O4 S
STATUS:	Actively Investigated
HIGHEST DEV. PHASE:	PHASE II
ORIGINATOR:	AstraZeneca National Cancer Institute (US)
CLASSIFICATION CODE:	Prostate Cancer Therapy
ACTION MECHANISM:	Endothelin ETA Receptor Antagonists; Antimitotic Drugs
OTHER SOURCE:	SYNTHLINE 2004000108
ENTRY DATE:	Entered STN: 9 May 2004 Last Updated on STN: 2 Jan 2007

STRUCTURE:



PROUS REFERENCES:

RefID: 705838 (Text Available)
Drug Data Report, Vol. 25, No. 1, pp 90, 2003

REFERENCE TEXT: RefID: 705838
ACTION - Potent and selective endothelin ETA receptor antagonist with low nanomolar affinity for ETA receptors and inactive at ETB receptors up to 10 mcM. In dogs, it inhibited the vasoconstriction mediated by ET-1 at 0.03 mg/kg i.v.; the inhibition produced by the dose of 0.1 mg/kg lasted for at least 7 h. Compound showed good oral bioavailability in rats and dogs (> 70%) and a favorable toxicity profile in rats. Potentially useful for the treatment of prostate cancer and metastatic bone disease. Currently in phase I clinical trials.

PATENT REFERENCES:

TITLE:	N-Heteroaryl-pyridinesulfonamide derivatives and their use as endothelin antagonists
INVENTOR(S):	Bradbury, R.H.; Butlin, R.J.; James, R.
PATENT ASSIGNEE(S):	AstraZeneca
PATENT INFORMATION:	EP 832082 19980401 JP 99509175 19990817 US 6060475 20000509 US 6258817 20010710 WO 9640681 19961219
PRIORITY INFORMATION:	GB 1995-11507 19950607 GB 1995-19666 19950927
TITLE:	Therapeutic use
INVENTOR(S):	Boyle, F.T.; Taylor, S.T.; Ashford, M.B.; Tonge, D.W.; Hughes, A.M.; Johnstone, D.; Barrass, N.C.
PATENT ASSIGNEE(S):	AstraZeneca
PATENT INFORMATION:	JP 2004083590 20040318 JP 2005097312 20050414 WO 2004018044 20040304
PRIORITY INFORMATION:	GB 2002-19660 20020823
TITLE:	Combination comprising N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4- (1,3,4-oxadiazol-2-yl)phenyl)pyridine-3-sulphonamide and an LHRH analogue and/or a bisphosphonate
INVENTOR(S):	Gallagher, N.
PATENT ASSIGNEE(S):	AstraZeneca
PATENT INFORMATION:	EP 1663236 20060607 US 2006287241 20061221

	WO 2005023264 20050317
PRIORITY INFORMATION:	GB 2003-20806 20030905
TITLE:	Therapeutic treatment
INVENTOR(S):	Boyle, F.T.; Taylor, S.T.; Curwen, J.O.; Tonge, D.W.; Hughes, A.M.; Johnstone, D.; Gallagher, N.J.; Hancox, U.J.
PATENT ASSIGNEE(S):	AstraZeneca
PATENT INFORMATION:	EP 1553950 20050720
	JP 2006510605 20060330
	US 2006122180 20060608
	WO 2004035057 20040429
PRIORITY INFORMATION:	GB 2002-23854 20021012
TITLE:	A combination of N-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-(1,3,4-oxadiazol-2-yl)phenyl)pyridine-3-sulphonamide and an anti-mitotic agent for the treatment of cancer
INVENTOR(S):	Boyle, F.T.; Johnstone, D.; Hughes, A.; Curwen, J.
PATENT ASSIGNEE(S):	AstraZeneca
PATENT INFORMATION:	WO 2006056760 20060601
PRIORITY INFORMATION:	GB 2004-25854 20041125

REFERENCES:

(1) RefID: 574545, Periodic Publication
"Zeneca ZD4054, an orally active endothelin-A receptor antagonist, prevents chronic hypoxia-induced pulmonary hypertension in the rat"
Bialecki, R.; et al., FASEB J, Vol. 14, No. 4, (Abst 115.16), 2000

(2) RefID: 702517, Periodic Publication
"ZD4054: A specific endothelin A receptor antagonist with potential utility in prostate cancer and metastatic bone disease"
Curwen, J.O.; Wilson, C., Eur J Cancer, Vol. 38, No. Suppl. 7, (Abst 340), 2002

(3) RefID: 834167, Periodic Publication
"ZD4054: Assessment of endothelin A receptor specificity following single dose administration in healthy volunteers"
Morris, C.; Wilson, D.; Hughes, A.; Le Maullf, F.; Brahma, S.; Fuhr, R., Eur J Cancer - Suppl, Vol. 2, No. 8, (Abst 76), 2004

(4) RefID: 834169, Periodic Publication
"ZD4054 specifically inhibits endothelin A receptor-mediated anti-apoptotic effects, but not endothelin B receptor-mediated pro-apoptotic effects"
Curtis, N.; Howard, Z.; Brooks, N.; Curwen, J., Eur J Cancer - Suppl, Vol. 2, No. 8, (Abst 78), 2004

(5) RefID: 884160, Congress Literature
"ZD4054 specifically inhibits endothelin A receptor-mediated effects, but not endothelin B receptor-mediated effects"
Dreicer, R.; Curtis, N.; Morris, C.; et al., Prostate Cancer Symp, Feb 17 2005-Feb 19 2005, Orlando, (Abst 237)

(6) RefID: 896857, Periodic Publication
"ZD4054 blocks ET-1-stimulated phosphorylation of p44/42 mitogen-activated kinase and proliferation of osteoblast cells"
Curtis, N.; Anderson, E.; Brooks, N.; Curwen, J., Proc Am Assoc Cancer Res (AACR), Vol. 46, (Abst 1512), 2005

(7) RefID: 912136, Periodic Publication
"Specific inhibition of the endothelin A receptor with ZD4054: Clinical and pre-clinical evidence"
Morris, C.D.; et al., Br J Cancer, Vol. 92, No. 12, pp 2148, 2005

(8) RefID: 928111, Congress Literature
"Tolerability profile of ZD4054 is consistent with the effects of endothelin A receptor-specific antagonism"
Liu, G.; Dreicer, R.; Hou, J.; Chen, Y.; Wilding, G., Annu Meet Am Soc Clin Oncol (ASCO) (41st Edition), May 13 2005-May 17 2005, Orlando, (Abst 4628)

(9) RefID: 931649, Periodic Publication
"ZD4054 reduces endothelin-1-induced forearm vasoconstriction in healthy male volunteers"
Morris, C.D.; Hughes, A.; Rose, A.; Melville, V.; Webb, D.J., Proc Am Assoc Cancer Res (AACR), Vol. 46, (Abst 4187), 2005

(10) RefID: 934253, Periodic Publication
"ZD4054, a specific antagonist of the endothelin A receptor, inhibits tumor growth and enhances cytotoxicity of paclitaxel in ovarian carcinoma in vitro and in vivo"
Rosano, L.; Di Castro, V.; Spinella, F.; Natali, P.G.; Bagnato, A., Proc Am Assoc Cancer Res (AACR), Vol. 46, (Abst 5830), 2005

(11) RefID: 1024585, Periodic Publication
"Proposed international nonproprietary names (Prop. INN): List 94"
WHO Drug Inf, Vol. 19, No. 4, pp 350, 2005

(12) RefID: 988596, Company Communication
"ZD4054 in pain-free or mildly symptomatic patients with prostate cancer and bone metastases who have rising serum prostate specific antigen (PSA) (NCT00090363)"
ClinicalTrials.gov Web Site, April 27, 2006

(13) RefID: 999673, Company Communication
"ZD4054/docetaxel combo study: Part A - dose finding, part B - randomized exploratory efficacy (NCT00314782)"
ClinicalTrials.gov Web Site, April 17, 2006

(14) RefID: 1044906, Periodic Publication
"Targeting bone metastasis in prostate cancer with endothelin receptor antagonists"
Carducci, M.A.; Jimeno, A., Clin Cancer Res, Vol. 12, No. 20, Part 2, pp 6296s, 2006

(15) RefID: 1050003, Congress Literature
"Combined targeting of the endothelin A receptor and the epidermal growth factor receptor enhances anti-tumor effects in ovarian carcinoma cells"
Bagnato, A.; Rosano, L.; Di Castro, V.; Spinella, F.; Nicotra, M.R.; Natali, P.G., Annu Meet Ital Cancer Soc (48th Edition), Oct 1 2006-Oct 4 2006, Bari, (Abst)

(16) RefID: 1052928, Periodic Publication
"The medical management of prostate cancer: A multidisciplinary team approach"
Sternberg, C.N.; Krainer, M.; Oh, W.K.; Bracarda, S.; Bellmunt, J.; Ozen, H.; Zlotta, A.; Beer, T.M.; Oudard, S.; Rauchenwald, M.; Skoneczna, I.; Borner, M.M.; Fitzpatrick, J.M., BJU Int, Vol. 99, No.

1, pp 22, 2006

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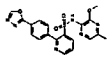
L9 ANSWER 35 OF 35 SYNTHLINE COPYRIGHT 2007 PROUS SCIENCE on STN

ACCESSION NUMBER:	2004:108 SYNTHLINE
ENTRY NUMBER:	258506
GENERIC NAME:	Zibotentan; ZD-4054
CHEMICAL NAME:	N-(3-Methoxy-5-methylpyrazin-2-yl)-2-(4-(1,3,4-oxadiazol-2-yl)phenyl)pyridine-3-sulfonamide
CAS REGISTRY NO.:	186497-07-4
MOLECULAR FORMULA:	C19 H16 N6 O4 S
MOLECULAR WEIGHT:	424.44
CLASSIFICATION CODE:	Genitourinary Cancer Therapy; Oncolytic Drugs; Prostate Cancer Therapy; Antimitotic Drugs; Endothelin ETA Receptor Antagonists
HIGHEST DEV. PHASE:	Phase II
STATUS:	Actively Investigated
COMPANY:	AstraZeneca; National Cancer Institute (US)
ENTRY DATE:	Entered STN: 16 Apr 2004 Last Updated on STN: 16 Jan 2007

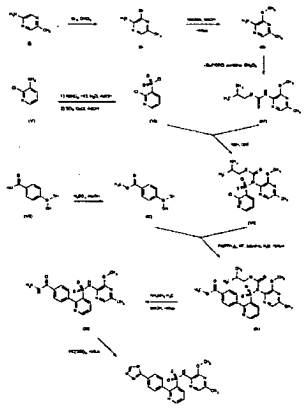
STRUCTURE:



REACTION: 25850601a

TEXT:

Bromination of 2-amino-5-methylpyrazine (I) with Br2 in CHCl3 affords the bromopyrazine (II). Subsequent bromide displacement in (II) by means of sodium methoxide gives rise to the methoxypyrazine (III). The amino group of (III) is then protected by acylation with isobutyl chloroformate, to produce carbamate (IV). Diazotization of 3-amino-2-chloropyridine (V), followed by treatment with sulfur dioxide in the presence of CuCl furnishes sulfonyl chloride (VI). Carbamate (IV) is then acylated by means of NaH and sulfonyl chloride (VI) in DMF to furnish the N-sulfonyl carbamate (VII). Esterification of 4-carboxyphenylboronic acid (VIII) with H2SO4 in MeOH gives 4-(methoxycarbonyl)phenylboronic acid (IX). Mitsunobu coupling between boronic acid (IX) and chloropyridine (VII) furnishes adduct (X). Methyl ester (X) is converted into hydrazide (XI) by treatment with hydrazine hydrate in refluxing methanol. Then, cyclization of the acyl hydrazide (XI) with boiling triethyl orthoformate gives rise to the target oxadiazole derivative.



TITLE:	N-Heteroaryl-pyridinesulfonamide derivs. and their use as endothelin antagonists
INVENTOR(S):	Bradbury, R.H.; Butlin, R.J.; James, R.
PATENT ASSIGNEE(S):	AstraZeneca plc
PATENT INFORMATION:	EP 832082; JP 99509175; US 6060475; US 6258817; WO 9640681
REACTANT IDENTIFIER:	(V) 11160
CHEMICAL NAME:	2-Chloro-3-aminopyridine; 2-Chloro-3-pyridinamine; 2-Chloro-3-pyridinylamine; 3-Amino-2-chloropyridine
CAS REGISTRY NO.:	6298-19-7
MOLECULAR FORMULA:	C5 H5 Cl N2
MOLECULAR WEIGHT:	128.56
COMPANY:	ABCR GmbH & Co.; Acros Organics; Aldrich; Alfa Aesar; Changzhou Hi-Tech Chemicals Limited; CMS Chemicals Limited; Combi-Blocks, Inc.; D&O Chemicals, Inc.; Eurolabs Limited; Fluka; Hebei Yanuo Chemical Industry Co., Ltd.; Koei Chemical Company, Ltd; Lancaster Synthesis Inc.; Lansdowne Chemicals Plc.; Maybridge Chemical Company, Ltd.; MP Biomedicals; Organix, Inc.; Pfaltz & Bauer, Inc.; Precursor Chemicals, Inc.; Runtec Chemical Co., Ltd.; Rutgers Organics; Syntesia Chemie GMBH; TCI; Unisource India; Xinchem Company
REACTANT IDENTIFIER:	(VIII) 32841
CHEMICAL NAME:	4-(dihydroxyboryl)benzoic acid
CAS REGISTRY NO.:	14047-29-1
MOLECULAR FORMULA:	C7 H7 B O4
MOLECULAR WEIGHT:	165.94
COMPANY:	Boron Molecular Pty Ltd; Charkit Chemical Corporation; Combi-Blocks, Inc.; Frontier Scientific, Inc.; Lancaster Synthesis Inc.; Optima Chemical Group LLC; Sanhe Chemport Chemicals Co.; TCI
REACTANT IDENTIFIER:	(I) 64109
CHEMICAL NAME:	5-methyl-2-pyrazinamine; 5-methyl-2-pyrazinylamine
MOLECULAR FORMULA:	C5 H7 N3
MOLECULAR WEIGHT:	109.13

REACTANT IDENTIFIER: (II) 64110
CHEMICAL NAME: 3-bromo-5-methyl-2-pyrazinamine; 3-bromo-5-methyl-2-pyrazinylamine
MOLECULAR FORMULA: C5 H6 Br N3
MOLECULAR WEIGHT: 188.03

REACTANT IDENTIFIER: (III) 64111
CHEMICAL NAME: 5-methyl-3-(methyloxy)-2-pyrazinamine; 5-methyl-3-(methyloxy)-2-pyrazinylamine
MOLECULAR FORMULA: C6 H9 N3 O
MOLECULAR WEIGHT: 139.16

REACTANT IDENTIFIER: (IV) 64112
CHEMICAL NAME: 2-methylpropyl 5-methyl-3-(methyloxy)-2-pyrazinylcarbamate
MOLECULAR FORMULA: C11 H17 N3 O3
MOLECULAR WEIGHT: 239.28

REACTANT IDENTIFIER: (VI) 64113
CHEMICAL NAME: 2-chloro-3-pyridinesulfonyl chloride
MOLECULAR FORMULA: C5 H3 Cl2 N O2 S
MOLECULAR WEIGHT: 212.06

REACTANT IDENTIFIER: (IX) 64114
CHEMICAL NAME: 4-((methyloxy)carbonyl)phenylboronic acid
CAS REGISTRY NO.: 99768-12-4
MOLECULAR FORMULA: C8 H9 B O4
MOLECULAR WEIGHT: 179.97
COMPANY: Frontier Scientific, Inc.; Matrix Scientific

REACTANT IDENTIFIER: (VII) 64115
CHEMICAL NAME: 2-methylpropyl (2-chloro-3-pyridinyl)sulfonyl(5-methyl-3-(methyloxy)-2-pyrazinyl)carbamate
MOLECULAR FORMULA: C16 H19 Cl N4 O5 S
MOLECULAR WEIGHT: 414.87

REACTANT IDENTIFIER: (X) 64116
CHEMICAL NAME: methyl 4-(3-(((5-methyl-3-(methyloxy)-2-pyrazinyl)(((2-methylpropyl)oxy)carbonyl)amino)sulfonyl)-2-pyridinyl)benzoate
MOLECULAR FORMULA: C24 H26 N4 O7 S
MOLECULAR WEIGHT: 514.56

REACTANT IDENTIFIER: (XI) 64117
CHEMICAL NAME: 2-(4-(hydrazinocarbonyl)phenyl)-N-(5-methyl-3-(methyloxy)-2-pyrazinyl)-3-pyridinesulfonamide
MOLECULAR FORMULA: C18 H18 N6 O4 S
MOLECULAR WEIGHT: 414.45

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L11 56 SEA ZIBOTENTAN# OR ZD4054 OR ZD 4054

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PROCESSING COMPLETED FOR L11
L12 39 DUP REM L11 (17 DUPLICATES REMOVED)
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ANSWERS '37-39' FROM FILE SCISEARCH

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L12 ANSWER 1 OF 39 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006628916 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17062717
TITLE: Targeting bone metastasis in prostate cancer with endothelin receptor antagonists.
AUTHOR: Carducci Michael A; Jimeno Antonio
CORPORATE SOURCE: Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland 21231-1000, USA.. carducci@jhmi.edu
SOURCE: Clinical cancer research : an official journal of the

American Association for Cancer Research, (2006 Oct 15) Vol. 12, No. 20 Pt 2, pp. 6296s-6300s. Ref: 44
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200611
ENTRY DATE: Entered STN: 26 Oct 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 29 Nov 2006

ABSTRACT:
Recent advances in the understanding of prostate cancer biology and its progression to bone metastasis have led to the development of drugs directed against precise molecular alterations in the prostate tumor cell and host cells in the normal bone environment such as osteoclasts and osteoblasts. Endothelins (ETs) and their receptors have emerged as a potential target in prostate cancer bone metastasis. By activating the ETA receptor, ET-1 is pathogenically involved in facilitating several aspects of prostate cancer progression, including proliferation, escape from apoptosis, invasion, and new bone formation, processes that are general to many malignancies. Notwithstanding, there are a number of features specifically driven by the ET axis in prostate cancer, such as creating and perpetuating a unique interaction between the metastatic prostate cancer cell and the bone microenvironment (osteoblast, osteoclast, and stroma) or altering the equilibrium in pain modulation. These features have led to the preferential clinical evaluation of atrasentan (ABT-627) as a biological therapy in prostate carcinoma, first in hormone-refractory prostate cancer. Biological activity of atrasentan in patients with prostate cancer has been shown by the suppression of biochemical markers of prostate cancer progression in bone, and clinical activity is evidenced by a consistent trend demonstrating a delay in time to disease progression when compared with placebo, especially in patients with bone metastases. Further studies of atrasentan and other selective ET-1 antagonists (ZD4054) are ongoing.

CONTROLLED TERM: Check Tags: Female; Male
*Antineoplastic Agents: TU, therapeutic use
*Bone Neoplasms: DT, drug therapy
*Bone Neoplasms: SC, secondary
Breast Neoplasms: PA, pathology
Clinical Trials
Humans
*Prostatic Neoplasms: PA, pathology
Pyrrolidines: TU, therapeutic use
*Receptors, Endothelin: AI, antagonists & inhibitors
CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Pyrrolidines); 0 (Receptors, Endothelin); 0 (ZD4054); 0 (atrasentan)

L12 ANSWER 2 OF 39 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006347879 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16741063
TITLE: ZD4054, a potent endothelin receptor A antagonist, inhibits ovarian carcinoma cell proliferation.
AUTHOR: Rosano Laura; Di Castro Valeriana; Spinella Francesca; Decandia Samantha; Natali Pier Giorgio; Bagnato Anna
CORPORATE SOURCE: Molecular Pathology Laboratory, Regina Elena Cancer Institute, Via delle Messi d'Oro 156, 00158 Rome, Italy.
SOURCE: Experimental biology and medicine (Maywood, N.J.), (2006 Jun) Vol. 231, No. 6, pp. 1132-5.

Journal code: 100973463. ISSN: 1535-3702.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200607
ENTRY DATE: Entered STN: 10 Jun 2006
Last Updated on STN: 6 Jul 2006
Entered Medline: 5 Jul 2006

ABSTRACT:
Endothelin-1 (ET-1) is present at high concentrations in ovarian cancer ascites and is overexpressed in primary and metastatic ovarian carcinomas. In these tumors, the presence of ET-1 correlates with tumor grade, enhanced neovascularization, and with vascular endothelial growth factor (VEGF) expression. ET-1 acts as an autocrine factor selectively through ET(A) receptor (ET(A)R), predominantly expressed in ovarian carcinoma cells resulting in increased VEGF production and VEGF-mediated angiogenic effects. Previous results demonstrated that in ovarian carcinoma cells, activation of the ET-1/ET(A)R axis promotes cell proliferation, neovascularization, and invasion, which are the principal hallmarks of tumor progression. The present study was designed to investigate the in vitro effects of trans, trans-2(4-methoxydhenyl)-4-(1-3-benzodiazol-5-yl)-1-(dibutylaminocarbonylmethyl)-pyrrolidine-3-carboxylic acid (ZD4054), an orally active specific ET(A)R antagonist, on the ET-1-induced mitogenic effect in OVCA 433 and HEY ovarian carcinoma cell lines secreting ET-1 and expressing ET(A)R and ET(B)R mRNA. We show that ET(A)R blockade by ZD4054 inhibits ET-1-induced mitogenic effects, while the ET(B)R antagonist, BQ 788, is ineffective. In conclusion, our data demonstrate that ZD4054 is capable in inhibiting the proliferative activity of ET-1, indicating that this specific ET(A)R antagonist may be a potential candidate in developing novel treatment of ovarian carcinoma.

CONTROLLED TERM: Check Tags: Female
Cell Line, Tumor
*Cell Proliferation: DE, drug effects
Endothelin-1: PD, pharmacology
*Endothelin-1: PH, physiology
Humans
*Ovarian Neoplasms: DT, drug therapy
Ovarian Neoplasms: ME, metabolism
Pyrrolidines: CH, chemistry
Pyrrolidines: PD, pharmacology
*Pyrrolidines: TU, therapeutic use
RNA, Messenger: ME, metabolism
*Receptor, Endothelin A: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
CHEMICAL NAME: 0 (Endothelin-1); 0 (Pyrrolidines); 0 (RNA, Messenger); 0 (Receptor, Endothelin A); 0 (ZD4054)

L12 ANSWER 3 OF 39 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2005308102 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15956965
TITLE: Specific inhibition of the endothelin A receptor with ZD4054: clinical and pre-clinical evidence.
AUTHOR: Morris C D; Rose A; Curwen J; Hughes A M; Wilson D J; Webb D J
CORPORATE SOURCE: AstraZeneca, Alderley Park, Macclesfield, Cheshire SK10 4TF, UK.. Clive.morris@astrazeneca.com
SOURCE: British journal of cancer, (2005 Jun 20) Vol. 92, No. 12, pp. 2148-52. Ref: 26
Journal code: 0370635. ISSN: 0007-0920.

PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 16 Jun 2005
Last Updated on STN: 13 Sep 2005
Entered Medline: 12 Sep 2005

ABSTRACT:
Activation of the endothelin A receptor (ET(A)) by endothelin-1 (ET-1) mediates events that regulate mitogenesis, apoptosis, angiogenesis and metastasis in tumours. Specific blockade of ET(A) may have anticancer effects, while retaining beneficial endothelin B receptor (ET(B))-mediated effects such as apoptosis and clearance of ET-1. ZD4054 is an orally active, specific ET(A) antagonist in clinical development. In receptor-binding studies, ZD4054 specifically bound to ET(A) with high affinity; no binding was detected at ET(B). In a randomised placebo-controlled trial in eight healthy volunteers, a single oral dose of ZD4054 reduced forearm vasoconstriction in response to brachial artery infusion of ET-1, thus providing clinical evidence of ET(A) blockade. ET(B) blockade was assessed in an ascending, single-dose, placebo-controlled trial in 28 volunteers. For all doses of ZD4054, mean plasma ET-1 concentrations measured at 4 and 24 h were within the placebo reference range (a rise in ET-1 would indicate ET(B) blockade) and there was no evidence of dose-related changes. These data confirm the specificity of ZD4054 for ET(A), with no activity at ET(B) in a clinical or preclinical setting. As a result of this specificity, ***ZD4054*** has the potential to block multiple ET(A)-induced pathological processes, while allowing beneficial ET(B)-mediated processes to continue, which may, in turn, lead to an effective cancer therapy.

CONTROLLED TERM: Animals
*Antineoplastic Agents: PD, pharmacology
Clinical Trials
Drug Evaluation, Preclinical
Endothelin-1: AI, antagonists & inhibitors
Endothelin-1: BL, blood
Humans
Radioligand Assay
*Receptor, Endothelin A: AI, antagonists & inhibitors
Receptor, Endothelin B: AI, antagonists & inhibitors
Research Support, Non-U.S. Gov't
Vasoconstriction: DE, drug effects

CHEMICAL NAME: 0 (Antineoplastic Agents); 0 (Endothelin-1); 0 (Receptor, Endothelin A); 0 (Receptor, Endothelin B)

L12 ANSWER 4 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN DUPLICATE 3
ACCESSION NUMBER: 2006-35607 DRUGU T Full-text
TITLE: Clinical trials of endothelin antagonists in heart failure: A question of dose
AUTHOR: Kelland N F; Webb D J
CORPORATE SOURCE: Univ.Edinburgh
LOCATION: Edinburgh, Midlothian, Scotland
SOURCE: ; Exp.Biol.&Med. (231, No. 6, 696-9, 2006) 1 Tab. 0 Ref.
CODEN: ; 3988
AVAIL. OF DOC.: Univ Edinburgh, Ctr Cardiovasc Sci, 3rd Floor,East Room E3-22,47 Little France Cresce, Edinburgh, Midlothian, Scotland, EH16 4TJ. (Webb D J, e-mail: d.j.webb@ed.ac.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

A review of clinical trials of endothelin (ET) antagonists in heart failure and their doses is presented. Topics covered are: the role of endothelin in chronic heart failure (CHF); the reasons why the clinical trials yielded negative results; and lessons that can be learned from the ET antagonists in CHF clinical trials. Drugs discussed are ET-1, bosentan, sitaxsentan, enrasentan, darusentan, BQ-788, BQ-123, ZD-4054, tezosentan and atrasentan. (No EX). (conference paper: 9th International Conference on Endothelin (ET-9), Park City, UT, USA, 11/09/2005-14/09/2005)

SECTION HEADING: T Therapeutics

CLASSIF. CODE: 58 Vasoactive
69 Reviews

CONTROLLED TERM:
CHRON. *TR; HEART-FAILURE *TR; CARDIOPATHY *TR; IN-VIVO *FT; CASES *FT; REVIEW *FT; ENDOTHELIN-ANTAGONIST *FT
[01] MAIN-TOPIC *FT; ENDOTHELIN-ANTAGONISTS *FT; TR *FT
[02] TR *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 5 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN DUPLICATE 4
ACCESSION NUMBER: 2006-35606 DRUGU T Full-text
TITLE: Profile of past and current clinical trials involving endothelin receptor antagonists: The novel "-sentan" class of drug.
AUTHOR: Battistini B; Berthiaume N; Kelland N F; Webb D J; Kohan D E
CORPORATE SOURCE: Univ.Laval; IPS-Pharma-Inc.; Univ.Edinburgh; Univ.Utah
LOCATION: St Foy, PQ, Canada
SOURCE: ; Exp.Biol.&Med. (231, No. 6, 653-95, 2006) 1 Fig. 7 Tab. 0 Ref.
CODEN: ; 3988
AVAIL. OF DOC.: Univ Laval, Ctr Rech,Dept Med, 2725 Chemin St Foy, St Foy, PQ, Canada, G1V 4G5. (Battistini B, e-mail: bruno.battistini@med.ulaval.ca).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

A review on the profile of past and current clinical trials involving endothelin (ET) receptor antagonists (ERAs; the novel-sentan class of drug). Topics covered are: the profile of ERAs used in preclinical studies and subsequent clinical academic studies and formal trials; approved new drug application (NDA)-the homologation of a new class of drug through clinical trials; formally completed and ongoing clinical academic studies and trials in control subjects and patients; completed clinical trials in control subjects and patients; and the safety and pharmacotoxicity of ERAs. Drugs discussed are BQ-123, BQ-788, bosentan, enrasentan, tezosentan, ambrisentan, atrasentan and avosentan. (conference paper: 9th International Conference on Endothelin (ET-9), Park City, UT, USA, 11/09/2005-14/09/2005)

SECTION HEADING: T Therapeutics

CLASSIF. CODE: 58 Vasoactive

69 Reviews
73 Trial Preparations

CONTROLLED TERM:
CARDIOPATHY *TR; PNEUMOPATHY *TR; IN-VIVO *FT; CASES *FT; REVIEW *FT; ENDOTHELIN-ANTAGONIST *FT; ENDOTHELIN-RECEPTOR *FT; RECEPTOR *FT
[01] MAIN-TOPIC *FT; ENDOTHELIN-ANTAGONISTS *FT; TR *FT
[02] BQ-123 *TR; BQ-788 *TR; BOSENTAN *TR; ENRASENTAN *TR; TEZOSENTAN *TR; AMBRISENTAN *TR; ATRASENTAN *TR; AVOSENTAN *TR; CLAZOSENTAN *TR; DARUSENTAN *TR; EDONENTAN *TR; SITAXSENTAN *TR; TBC-3711 *TR; ZD-4054 *TR; YM-598 *TR; BMS-193884 *TR; LU-208075 *TR; LU-302146 *TR; RO-61-1790 *TR; LU-135252 *TR; TAK-044 *TR; S-0139 *TR; A-192621 *TR; SARAFOTOXIN-S6C *TR; ENDOTHELIN-1 *TR; TR *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 6 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-41082 DRUGU P B Full-text
TITLE: Combined targeting of the endothelin A receptor and the epidermal growth factor receptor in ovarian cancer shows enhanced antiproliferative effects.
AUTHOR: Rosano L; Di Castro V; Spinella F; Natali P G; Bagnato A
CORPORATE SOURCE: Regina-Elena-Inst.Rome
LOCATION: Rome, Italy
SOURCE: Proc.Am.Assoc.Cancer Res. (47, Abs1509, 2006) 0 Ref.
ISSN: 0197-016X
AVAIL. OF DOC.: Regina Elena Canc Inst, Mol Pathol Lab, Rome, Italy.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

This study examined in-vitro (HEY and OVCA 433 ovarian carcinoma cell lines) and in-vivo (mice) the effect of ZD-4054 (zibotenan), a potent specific endothelin A receptors (ETAR) antagonist, as mono and combination therapy with the selective EGF receptor (EGFR) tyrosine kinase inhibitor, gefitinib (GF, Iressa). ZD-4054 is a candidate for clinical testing as an antitumor agent in ovarian cancer patients, either as monotherapy or in combination with GF. The cross-signaling between the EGFR/ETAR pathways along with the emerging role of ET-1 axis in ovarian tumorigenesis and progression provided a rationale to combine EGFR tyrosine kinase inhibitors with ETAR antagonists for cancer treatment. (conference abstract: 97th Annual Meeting of the American Association for Cancer Research, Washington, DC, USA, 01/04/2006-05/04/2006)

SECTION HEADING: P Pharmacology
B Biochemistry

CLASSIF. CODE: 14 Enzyme Inhibitors
27 Molecular Biology
52 Chemotherapy - non-clinical
66 Drug Interactions

CONTROLLED TERM:
IN-VIVO *FT; IN-VITRO *FT; MOUSE *FT; HEY-CELL *FT; OVCA433-CELL *FT; ALONE *FT; COMB. *FT; CYTOSTATIC *FT; MODE-OF-ACT. *FT; VEGF-ANTAGONIST *FT; APOPTOSIS *FT;

APOPTOSIS-INDUCER *FT; REGRESSION *FT; PARTIAL *FT; COMPLETE *FT; MAP-KINASE-INHIBITOR *FT; LAB.ANIMAL *FT; ADENOCARCINOMA *FT; TUMOR-CELL *FT; TISSUE-CULTURE *FT
[01] ZIBOTENAN *PH; ZIBOTENAN *DI; DR0019173 *RN; GEFITINIB *DI; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; SYNERGISTS *FT; VASODILATORS *FT; HYPOTENSIVES *FT; I.P. *FT; ENDOTHELIN-ANTAGONIST *FT; INJECTION *FT; PH *FT; DI *FT
[02] GEFITINIB *PH; GEFITINIB *DI; DR9703865 *RN; IRESSA *PH; IRESSA *PH; IRESSA *DI; IRESSA *DI; ZIBOTENAN *DI; CYTOSTATICS *FT; TYROSINE-KINASE-INHIBITORS *FT; ANGIOGENESIS-INHIBITORS *FT; APOPTOSIS-INDUCERS *FT; RADIOSENSITIZERS *FT; EPIDERMAL-GROWTH-FACTOR-ANTAGONISTS *FT; P.O. *FT; EPIDERMAL-GROWTH-FACTOR-ANTAGONIST *FT; PH *FT; DI *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 7 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-32557 DRUGU P B Full-text
TITLE: ZD4054, a specific antagonist of the endothelin A receptor, inhibits tumor growth and enhances cytotoxicity of paclitaxel in ovarian carcinoma in vitro and in vivo.
AUTHOR: Rosano L; Di Castro V; Spinella F; Natali P G; Bagnato A
CORPORATE SOURCE: Regina-Elena-Inst.Rome
LOCATION: Rome, It.
SOURCE: Proc.Am.Assoc.Cancer Res. (96 Meet., 5830, 2005) ISSN: 0197-016X
AVAIL. OF DOC.: Regina Elena Cancer Institute, Rome, Italy. (A.B.).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

ZD-4054 inhibited tumor growth and enhanced cytotoxicity of paclitaxel on ovarian carcinoma cells in-vitro and in athymic nude mouse xenograft models. This endothelin A receptor antagonist may be a candidate for clinical trials as an antitumor agent in ovarian cancer patients, either as a single agent or in combination with taxane therapy. (conference abstract: 96th Annual Meeting of the American Association for Cancer Research, Anaheim, California, USA, April 16-20, 2005).

SECTION HEADING: P Pharmacology
B Biochemistry

CLASSIF. CODE: 27 Molecular Biology
52 Chemotherapy - non-clinical
66 Drug Interactions
73 Trial Preparations

CONTROLLED TERM:
OVARY *OC; ADENOCARCINOMA *OC; OVARY-DISEASE *OC; ANIMAL-NEOPLASM *OC; MOUSE *FT; IN-VIVO *FT; ATHYMIC *FT; NUDE *FT; XENOGRAFT *FT; HEY-CELL *FT; OVCA433-CELL *FT; TUMOR-CELL *FT; CYTOSTATIC *FT; SYNERGIST *FT; LAB.ANIMAL *FT; TISSUE-CULTURE *FT
[01] ZD-4054 *PH; ZD-4054 *DI; DR0019173 *RN; PACLITAXEL *DI; I.P. *FT; ENDOTHELIN-ANTAGONIST *FT; ENDOTHELIN-A *FT; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; HYPOTENSIVES *FT; SYNERGISTS *FT;

TRIAL-PREP. *FT; VASODILATORS *FT; INJECTION *FT; PH *FT; DI *FT
[02] PACLITAXEL *PH; PACLITAXEL *DI; ZD-4054 *DI; TAXOL *RN; I.V. *FT; APOPTOSIS-INDUCER *FT; APOPTOSIS *FT; INJECTION *FT; CYTOSTATICS *FT; P-GLYCOPROTEIN-INHIBITORS *FT; PH *FT; DI *FT
CAS REGISTRY NO.: 33069-62-4
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 8 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-42068 DRUGU T S Full-text
TITLE: Tolerability profile of ZD4054 is consistent with the effects of endothelin A receptor-specific antagonism.
AUTHOR: Liu G; Dreicer R; Hou J; Chen Y; Wilding G
CORPORATE SOURCE: Univ.Wisconsin; Cleveland-Clin.Found.; AstraZeneca
LOCATION: Madison, WI, Cleveland, OH; Wilmington, DE, USA
SOURCE: J.Clin.Oncol. (23, No. 16, Suppl., 4628, 2005)
CODEN: JCONDN ISSN: 0732-183X
AVAIL. OF DOC.: University of Wisconsin, Madison, WI, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

ZD-4054 is an active, potent and specific endothelin A receptor antagonist with anticancer activity. The Authors aimed to assess the tolerability of ZD-4054 in 16 patients with hormone refractory prostate cancer (HRPC), after p.o. dosing. ZD-***4054*** was well tolerated. The maximum tolerated dose (MTD) was 15 mg. ***ZD*** -4054 has the potential to block the pathological processes in malignancy that are mediated by endothelin A, while allowing the beneficial processes mediated by endothelin B to proceed. (conference abstract: 41st Annual Meeting of the American Society of Clinical Oncology, Orlando, Florida, USA, May 13-17, 2005).

SECTION HEADING: T Therapeutics
S Adverse Effects

CLASSIF. CODE: 35 Adverse Reactions
51 Chemotherapy - clinical
64 Clinical Trials
73 Trial Preparations

CONTROLLED TERM:
[01] ZD-4054 *TR; ZD-4054 *AE; DR0019173 *RN; PROSTATE *TR; NEOPLASM *TR; PROSTATE-DISEASE *TR; DYSPNEA *AE; EDEMA *AE; HEADACHE *AE; HEMORRHAGE *AE; ASTHENIA *AE; NAUSEA *AE; CONGESTION *AE; RESPIRATION-DISORDER *AE; CASES *FT; IN-VIVO *FT; P.O. *FT; CYTOSTATIC *FT; PROGNOSIS *FT; PHASE-II *FT; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; HYPOTENSIVES *FT; SYNERGISTS *FT; TRIAL-PREP. *FT; VASODILATORS *FT; CLIN.TRIAL *FT; TR *FT; AE *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 9 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-32525 DRUGU P Full-text

TITLE: ZD4054 reduces endothelin-1-induced forearm vasoconstriction in healthy male volunteers.
AUTHOR: Morris C D; Hughes A; Rose A; Melville V; Webb D J
CORPORATE SOURCE: AstraZeneca; Univ.Edinburgh
LOCATION: Macclesfield; Edinburgh, U.K.
SOURCE: Proc.Am.Assoc.Cancer Res. (96 Meet., 4187, 2005) 2 Ref.
ISSN: 0197-016X
AVAIL. OF DOC.: AstraZeneca Pharmaceuticals, Macclesfield, England.
LANGUAGE: English .
DOCUMENT TYPE: Journal

ABSTRACT:

The effect of a single, p.o. dose of ZD-4054 on blockade of forearm vasoconstriction in response to brachial artery infusion of endothelin-1 (ET-1) was assessed in a single dose, placebo-controlled, double-blind, randomized study of 8 healthy male volunteers. Results suggest that ZD-4054 is a specific endothelin A receptor (ETA) antagonist in man. Since ET-1, acting through ETA, may be an important driver of oncogenesis, these results provide a rationale for further evaluation of ***ZD*** -4054 as a cancer therapy. (conference abstract: 96th Annual Meeting of the American Association for Cancer Research, Anaheim, California, USA, April 16-20, 2005).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 58 Vasoactive
64 Clinical Trials
73 Trial Preparations

CONTROLLED TERM:
[01] ZD-4054 *PH; DR0019173 *RN; HUMAN *FT; IN-VIVO *FT; P.O. *FT; PLACEBO *FT; DOUBLE *FT; BLIND-TEST *FT; RANDOM *FT; CLIN.TRIAL *FT; VASOCONSTRICTION *FT; BLOOD-FLOW *FT; ENDOTHELIN-A *FT; ENDOTHELIN-ANTAGONIST *FT; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; HYPOTENSIVES *FT; SYNERGISTS *FT; TRIAL-PREP. *FT; VASODILATORS *FT; CLIN.TRIAL *FT; HEMODYNAMICS *FT; PH *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 10 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-31712 DRUGU P Full-text
TITLE: ZD4054 blocks ET-1-stimulated phosphorylation of p44/42 mitogen-activated kinase and proliferation of osteoblast cells.
AUTHOR: Curtis N; Anderson E; Brooks N; Curwen J
CORPORATE SOURCE: AstraZeneca
LOCATION: Macclesfield, U.K.
SOURCE: Proc.Am.Assoc.Cancer Res. (96 Meet., 1512, 2005) ISSN: 0197-016X
AVAIL. OF DOC.: AstraZeneca Pharmaceuticals, Macclesfield, England.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The effect of ZD-4054 on phosphorylation of p44/42 MAPK in

murine osteoblast MC3T3.E1/J1 cells and on the proliferation of human immature pre-osteoblast HCB-171 cells was investigated in-vitro. ZD-***4054*** blocked ETA-mediated activation of p44/p42 MAPK in murine osteoblast cells and proliferation of human immature pre-osteoblast cells. ***ZD*** -4054 has the potential to inhibit tumor induced ET-1-stimulated bone remodeling and autocrine ET-1-driven bone remodeling in metastatic bone cancer. (conference abstract: 96th Annual Meeting of the American Association for Cancer Research, Anaheim, California, USA, April 16-20, 2005).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 24 Bones and Joints
52 Chemotherapy - non-clinical
73 Trial Preparations

CONTROLLED TERM:
[01] ZD-4054 *PH; DR0019173 *RN; IN-VITRO *FT; OSTEOBLAST *FT; TISSUE-CULTURE *FT; PROLIFERATION *FT; TRIAL-PREP. *FT; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; HYPOTENSIVES *FT; SYNERGISTS *FT; VASODILATORS *FT; BONE *FT; PH *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 11 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-05157 DRUGU P Full-text
TITLE: ZD4054 specifically inhibits endothelin A receptor-mediated anti-apoptotic effects, but not endothelin B receptor-mediated pro-apoptotic effects.
AUTHOR: Curtis N; Howard Z; Brooks N; Curwen J
CORPORATE SOURCE: AstraZeneca
LOCATION: Macclesfield, U.K.
SOURCE: Eur.J.Cancer Suppl. (2, No. 8, 27, 2004) ISSN: 1359-6349
AVAIL. OF DOC.: AstraZeneca, Macclesfield, England.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The effect of ZD-4054 on endothelin-A (ETA) and endothelin B (ETB) receptor-mediated anti-apoptotic effects were studied. ZD-***4054*** inhibited ETA-mediated anti-apoptotic events while allowing pro-apoptotic signaling via ETB in both human and rat epithelial cell lines in vitro. ZD-4054 has the potential to block the pathological processes mediated by the ETA receptor, but allow the beneficial processes mediated by the ETB receptor to proceed. (conference abstract: 16th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, Geneva, Switzerland, September 28-October 1, 2004).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 52 Chemotherapy - non-clinical
73 Trial Preparations

CONTROLLED TERM:
[01] ZD-4054 *PH; DR0019173 *RN; IN-VITRO *FT; RAT *FT; HUMAN *FT; EPITHELIUM *FT; TISSUE-CULTURE *FT;

ENDOTHELIN-ET-A-ANTAGONIST *FT; CYTOSTATIC *FT; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; HYPOTENSIVES *FT; TRIAL-PREP. *FT; VASODILATORS *FT; ENDOTHELIN-ET-A-ANTAGONISTS *FT; LAB.ANIMAL *FT; PH *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 12 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-05155 DRUGU P Full-text
TITLE: ZD4054: assessment of endothelin A receptor specificity following single dose administration in healthy volunteers.
AUTHOR: Morris C; Wilson D; Hughes A; Le Maulf F; Brahma S; Fuhr R
CORPORATE SOURCE: AstraZeneca; Parexel
LOCATION: Macclesfield, U.K.; Berlin, Ger.
SOURCE: Eur.J.Cancer Suppl. (2, No. 8, 26, 2004) ISSN: 1359-6349
AVAIL. OF DOC.: AstraZeneca, Macclesfield, England.
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

Endothelin A (ETA) receptor specificity following single dose administration of ***ZD*** -4054 was assessed in 50 healthy volunteers in a randomized, ascending, double-blind, placebo-controlled study. Results confirm the preclinical findings that ZD-4054 specifically antagonizes ETA, with no evidence for inhibition of ETB and ZD4054 has the potential to block the pathological processes in malignancy that are mediated by ETA while allowing the beneficial processes mediated by ETB to proceed. (conference abstract: 16th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, Geneva, Switzerland, September 28-October 1, 2004).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 51 Chemotherapy - clinical
63 Receptors
64 Clinical Trials
73 Trial Preparations

CONTROLLED TERM:
[01] ZD-4054 *PH; DR0019173 *RN; CASES *FT; IN-VIVO *FT; RANDOM *FT; DOUBLE *FT; BLIND-TEST *FT; PLACEBO *FT; CLIN.TRIAL *FT; ENDOTHELIN-ET-A-RECEPTOR *FT; ENDOTHELIN-RECEPTOR *FT; SPECIFICITY *FT; ENDOTHELIN-ET-A-ANTAGONIST *FT; CYTOSTATICS *FT; ENDOTHELIN-ANTAGONISTS *FT; HYPOTENSIVES *FT; TRIAL-PREP. *FT; VASODILATORS *FT; ENDOTHELIN-ET-A-ANTAGONISTS *FT; CLIN.TRIAL *FT; RECEPTOR *FT; PH *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L12 ANSWER 13 OF 39 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 111291 DRUGU
FILE SEGMENT: Registry
DERWENT DRUG REGISTRY NAME: DR0019173
DERWENT DRUG NAME: ZIBOTENTAN
CONTROLLED TERM: CYTOSTATICS; ENDOTHELIN-ANTAGONISTS; SYNERGISTS;

VASODILATORS; HYPOTENSIVES
SUBSTRUCTURE TERM: AMIDINE,CYCLIC; PYRIDINE; SULFONAMIDE; PYRAZINE; BH-LINKED-CC; IMIDATE; OXADIAZOLE

L12 ANSWER 14 OF 39 PASCAL COPYRIGHT 2007 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2007-0018616 PASCAL Full-text
COPYRIGHT NOTICE: Copyright .COPYRGT. 2007 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Targeting bone metastasis in prostate cancer with endothelin receptor antagonists
Advances in treating metastatic bone cancer: Proceedings of the first Cambridge conference
AUTHOR: CARDUCCI Michael A.; JIMENO Antonio
LIPTON Allan (ed.); BERENSON James R. (ed.); COLEMAN Robert E. (ed.); COOK Richard J. (ed.); GUISE Theresa A. (ed.); SMITH Matthew R. (ed.)
CORPORATE SOURCE: Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland, United States
Penn State University, College of Medicine, Milton S. Hershey Medical Center, West Hollywood, CA, United States; Institute for Myeloma and Bone Cancer Research, West Hollywood, CA, United States; Cancer Research Centre Weston Park Hospital, Academic Unit of Clinical Oncology, Sheffield, United Kingdom; University of Waterloo, Department of Statistics and Actuarial Science, Waterloo, Ontario, Canada; University of Virginia, Charlottesville, Virginia, United States; Cancer Center, Division of Hematology Oncology, Boston, MA, United States
SOURCE: Clinical cancer research, (2006), 12(20, p. 2), 6296s-6300s, 44 refs.
Conference: 1 Cambridge Conference on Advances in Treating Metastatic Bone Cancer, Cambridge, Massachusetts (United States), 28 Oct 2005-29 Oct 2005
ISSN: 1078-0432
DOCUMENT TYPE: Journal; Conference
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-26073, 354000158813790160
ABSTRACT: Recent advances in the understanding of prostate cancer biology and its progression to bone metastasis have led to the development of drugs directed against precise molecular alterations in the prostate tumor cell and host cells in the normal bone environment such as osteoclasts and osteoblasts. Endothelins (ETs) and their receptors have emerged as a potential target in prostate cancer bone metastasis. By activating the ETA receptor, ET-1 is pathogenically involved in facilitating several aspects of prostate cancer progression, including proliferation, escape from apoptosis, invasion, and new bone formation, processes that are general to many malignancies. Notwithstanding, there are a number of features specifically driven by the ETaxis in prostate cancer, such as creating and perpetuating a unique interaction between the metastatic prostate cancer cell and the bone microenvironment (osteoblast, osteoclast, and stroma) or altering the equilibrium in pain modulation. These features have led to the preferential clinical evaluation of atrasentan (ABT-627) as a biological therapy in prostate carcinoma, first in hormone-refractory prostate cancer. Biological activity of atrasentan in patients with prostate cancer has been shown by the suppression of biochemical markers of prostate cancer progression in bone, and clinical activity is evidenced by a consistent trend demonstrating a delay in time to disease progression when compared with placebo, especially in patients with bone

metastases. Further studies of atrasentan and other selective ET-1 antagonists (ZD4054) are ongoing. CLASSIFICATION CODE: 002B02R; Life sciences; Medical sciences;
Pharmacology; Oncology
002B15C; Life sciences; Medical sciences; Bone and joint diseases, Musculoskeletal system; Oncology
002B14D02; Life sciences; Medical sciences; Nephrology, Urinary system; Oncology
002B20B02; Life sciences; Medical sciences; Andrology, Genital system; Oncology
CONTROLLED TERM: Target; Targeting; Prostate cancer; Endothelin receptor; Antagonist; Bone metastasis
BROADER TERM: Diseases of the osteoarticular system; Malignant tumor; Male genital diseases; Urinary system disease; Prostate disease

L12 ANSWER 15 OF 39 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-414359 [42] WPIX
DOC. NO. CPI: C2006-130699 [42]
TITLE: Pharmaceutical composition useful for treating congestive heart failure comprises phosphodiesterase V inhibitor compound, ETA receptor antagonist, and excipient
DERWENT CLASS: B02
INVENTOR: CUFFIE-JACKSON C; VELTRI E P
PATENT ASSIGNEE: (SCHE-C) SCHERING CORP
COUNTRY COUNT: 111

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006055573	A2	20060526	(200642)*	EN	145[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006055573	A2	WO 2005-US41386	20051116

PRIORITY APPLN. INFO: US 2004-629030P 20041118
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0031-422 [I,A]; A61K0031-519 [I,C]; A61K0031-522 [I,A]; A61P0009-00 [I,C]; A61P0009-04 [I,A]
BASIC ABSTRACT:
WO 2006055573 A2 UPAB: 20060703
NOVELTY - A pharmaceutical composition comprises a phosphodiesterase V (PDE V) inhibitor compound, an ETA receptor antagonist, and an excipient.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of PDE V inhibitor compound of formula (I), its enantiomer, stereoisomer, rotomer, tautomer or salt in the preparation of a medicament for treating congestive heart failure. R1 = 1-15C alkyl, 2-15C alkenyl, 2-15C alkynyl (all optionally branched and at least mono-substituted by T1) or H; R2 = 1-15C alkyl, 2-15C alkenyl, 2-15C alkynyl (all optionally branched and at least mono-substituted by T1) or H; R3 = (hetero)aryl (optionally at least mono-substituted by T1), or a heterocyclic group having 1 - 3 heteroatoms fused to a 5- or 6-membered aryl ring (optionally at least mono-substituted by T1); Y = a C-C single bond, -CO-, -O-, -S- -N(R21)-, -CON(R22)-, -N(R22)CO-, -OCH2-, -CH2O-, -SCH2-, -

CH2S-, -NHC(R23)(R24)-, -N(R23)SO2-, -SO2N(R23)-, -R23R24NH-, -CH=CH-, -CF=CF-, -CH=CF-, -CF=CH-, -CH2CH2, -CF2CF2, cyclopropan-1,2-diyl, cyclopropan-1,1-diyl, -CH(OR25)-, -CH(OCOR26)-, -C=(NR27)- or -C(OR28)(OR29)-; R21 = H or -CO(1-4C alkyl), 1-6C alkyl, allyl, 3-6C cycloalkyl, phenyl or benzyl group;
R22 = H or 1-6C alkyl;
R23 = H, 1-6C alkyl, aryl or -CH2-aryl; R24 = H or 1-4C alkyl;
R25 = H, 3-6C cycloalkyl, 1-8C (perfluoro)alkyl, phenyl or benzyl; R26 = H, 1-6C alkyl, 3-6C cycloalkyl, phenyl or benzyl; R27 = -NR23R24, OR24, -NHCONH2, -NHCSNH2, -NHSO2(4-methylphenyl) or -NHSO2phenyl;
R28, R29 = 1-4C alkyl;
R28+R29 = -(CH2)q;
q = 2 or 3;
R4 = 3-15C cycloalkyl or 3-15C cycloalkenyl (both optionally at least mono-substituted by T1);
T1 = (cyclo)alkyl, (cyclo)alkenyl, alkynyl, arylalkyl, alkylaryl, (hetero)aryl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, haloalkyl, thioalkyl, alkylthioalkyl, carboxyalkyl, imidazolylalkyl, indolylalkyl, mono-, di- and trihaloalkyl, mono-, di- and trihaloalkoxy, amino, (di)alkylamino, alkoxy, hydroxy, halo, nitro, oximino, -COOR50, -COR50, -SO0-2R50, -SO2NR50R51, -NR52SO2R50, =C(R50R51), =N-OR50, =N-CN, =C(halo)2, =S, =O, -CON(R50R51), -OCOR50, -OCON(R50R51), -N(R52)CO(R50), -N(R52)COOR50 or -N(R52)CON(R50R51); R50 - R52 = 1-6C alkyl, 3-6C cycloalkyl, 4-6C heterocycloalkyl, (hetero)aryl (all optionally branched and substituted), phenyl, pyridinyl, pyridazin-4-yl, pyrimidin-5-yl, pyrazine, piperidinyl, thiophenyl (all seven disubstituted by R40 and R41), H, (1,3,5)triazin-2-yl (substituted at 4 and 6 positions by R40 and R41, respectively), imidazolyl (substituted at 1-position by R43, and also disubstituted by R40 and R41), 2H-tetrazol-5-yl (substituted at 2-position by R43), 1H-tetrazol-5-yl (substituted at 1-position by R43) or 2H-tetrazolyl (mono-substituted by R40);
R50+R51 = a carbocyclic or heterocyclic ring system; R40, R41 = alkyl, cycloalkyl, (hetero)cycloalkyl, halo, imidazolylalkyl, indolylalkyl, (hetero)aryl, (hetero)arylalkyl, (hetero)arylalkoxy, aminoalkyl, haloalkyl, mono-, di- or trihaloalkyl, mono-, di- or trihaloalkoxy, nitro, cyano, alkoxy, hydroxy, amino, phosphino, phosphate, formyl, (di)alkylamino, alkylthio, trialkylsilyl, alkylsulfonyl, arylsulfonyl, alkylsulfinyl, aminoalkyl, (di)alkylaminoalkyl, hydroxyalkyl, morpholino, thioalkyl, alkylthioalkyl, carboxyalkyl, oximino, -COOR50, -COR50, -SO0-2R50, -SO2NR50R51, -NR52SO2R50, -CON(R50R51), -OCON(R50R51), -N(R52)CO(R50), -N(R52)COOR50, -N(R52)CON(R50R51) or -OCONR50 (all optionally branched and substituted) or H;
R42 = alkyl, alkenyl, arylalkyl or acyl group (all optionally branched and substituted) or H; and R43 = alkyl or aryl (both optionally branched and substituted) or H.
Provided that R3 is not an aryl group substituted at its para position with a -Y-aryl group.
ACTIVITY - Antiarteriosclerotic; Cardiant; Cardiovascular-Gen.; Antiarrhythmic; Cerebroprotective; Vasotropic; Thrombolytic; Antiinflammatory; Antimigraine; Nephrotropic.
MECHANISM OF ACTION - Phosphodiesterase V receptor inhibitor; ETA receptor antagonist.
Tests showed that 8-cyclopentylamino-1,3-diethyl-7-(4-methoxy- benzyl)-3,7-dihydro-purine-2,6-dione exhibited a PDE V IC50 of 5 nM or less.
USE - For the preparation of a medicament for treating congestive heart failure (claimed); also for treating atherosclerosis, acute coronary syndrome, arrhythmia, heart disease, myocardial infarction, thrombotic or thromboembolytic stroke, a deep vein thrombosis, venous thromboembolism, a cardiovascular disease associated with hormone replacement therapy, disseminated intravascular coagulation syndrome, renal ischemia, cerebral stroke, cerebral ischemia, cerebral infarction, migraine, or renal vascular homeostasis.
ADVANTAGE - The composition possesses superior therapeutic properties.

MANUAL CODE: CPI: B05-B01M; B05-B02C; B06-A02; B06-D09; B07-D12; B14-C01; B14-D03; B14-D07A1; B14-F01; B14-F02; B14-F04; B14-F07; B14-L01; B14-L06; B14-N10; B14-N16

TECH
PHARMACEUTICALS - Preferred Method: The method further involves use of at least one additional therapeutic agent and at least one ETA receptor antagonist in the preparation of the medicament.
Preferred Components: The additional therapeutic agent is selected from prostanoids, alpha-adrenergic receptor, dopamine receptor agonists, melanocortin receptor agonists, endothelin receptor antagonists, endothelin converting enzyme inhibitors, angiotensin II receptor antagonists, angiotensin converting enzyme inhibitors, neutral metalloendopeptidase inhibitors, renin inhibitors, serotonin 5-HT2c receptor agonists, nociceptin receptor agonists, rho kinase inhibitors, potassium channel modulators and inhibitors of multidrug resistance protein 5. The ETA receptor antagonist is selected from bosentan, atrasentan, ambrisentan, darusentan, sitaxsentan, ABT-627, TBC-3711, CI-1034, SPP-301, SB-234551, ZD-4054, BQ-123 and BE-18257B (preferably sitaxsentan).

L12 ANSWER 16 OF 39 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-365095 [34] WPIX
DOC. NO. CPI: C2004-137842 [34]
TITLE: Combination, useful in the manufacture of a medicament for the treatment of cancer e.g. esophageal cancer, comprises endothelin receptor antagonist and an epidermal growth factor receptor tyrosine kinase inhibitor
DERWENT CLASS: B05
INVENTOR: BOYLE F T; CURWEN J O; GALLAGHER N J; HANCOX U J; HUGHES A M; JOHNSTONE D; TAYLOR S T; TONGE D W
PATENT ASSIGNEE: (ASTR-C) ASTRAZENECA AB; (ASTR-C) ASTRAZENECA UK LTD; (BOYL-I) BOYLE F T; (CURW-I) CURWEN J O; (GALL-I) GALLAGHER N J; (HANC-I) HANCOX U J; (HUGH-I) HUGHES A M; (JOHN-I) JOHNSTONE D; (TAYL-I) TAYLOR S T; (TONG-I) TONGE D W
COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004035057	A1	20040429	(200434)*	EN	24[3]	
AU 2003269259	A1	20040504	(200467)	EN		
NO 2005001658	A	20050506	(200537)	NO		A61K045-06
EP 1553950	A1	20050720	(200547)	EN		
BR 2003015140	A	20050816	(200557)	PT		
TW 2004012971	A	20040801	(200581)	ZH		
ZA 2005002874	A	20060222	(200619)	EN	32	A61K000-00
JP 2006510605	W	20060330	(200623)	JA	18	
US 20060122180	A1	20060608	(200639)	EN		
KR 2005056238	A	20050614	(200641)	KO		A61K031-517

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004035057	A1	WO 2003-GB4347	20031007
AU 2003269259	A1	AU 2003-269259	20031007
BR 2003015140	A	BR 2003-15140	20031007
EP 1553950	A1	EP 2003-751038	20031007

NO 2005001658 A		WO 2003-GB4347 20031007
EP 1553950 A1		WO 2003-GB4347 20031007
BR 2003015140 A		WO 2003-GB4347 20031007
JP 2006510605 W		WO 2003-GB4347 20031007
US 20060122180 A1		WO 2003-GB4347 20031007
TW 2004012971 A		TW 2003-128113 20031009
JP 2006510605 W		JP 2004-544431 20031007
NO 2005001658 A		NO 2005-1658 20050404
US 20060122180 A1		US 2005-530794 20050408
ZA 2005002874 A		ZA 2005-2874 20050408
KR 2005056238 A		WO 2003-GB4347 20031007
KR 2005056238 A		KR 2005-706232 20050411

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003269259	A1	Based on	WO 2004035057	A
EP 1553950	A1	Based on	WO 2004035057	A
BR 2003015140	A	Based on	WO 2004035057	A
JP 2006510605	W	Based on	WO 2004035057	A
KR 2005056238	A	Based on	WO 2004035057	A

PRIORITY APPLN. INFO: GB 2002-23854 20021012
INT. PATENT CLASSIF.:
MAIN: A61K; A61K031-517; A61K045-06
SECONDARY: A61K045-00; A61P035-04; A61K031-497; A61K031-4985
IPC ORIGINAL: A61K0031-357 [I,C]; A61K0031-36 [I,A]; A61K0031-4025 [I,A]; A61K0031-42 [I,A]; A61K0031-422 [I,A]; A61K0031-47 [I,A]; A61K0031-4965 [I,C]; A61K0031-4965 [I,A]; A61K0031-497 [I,A]; A61K0031-505 [I,A]; A61K0031-517 [I,A]; A61K0031-519 [I,A]; A61K0031-5375 [I,A]; A61K0031-5375 [I,C]; A61K0031-5377 [I,A]; A61K0045-00 [I,C]; A61K0045-06 [I,A]; A61P0035-00 [I,A]; A61P0035-04 [I,A]; A61P0043-00 [I,A]
IPC RECLASSIF.: A61K0031-517 [I,A]; A61K0031-517 [I,C]; A61K0045-00 [I,C] ; A61K0045-06 [I,A]

BASIC ABSTRACT:
WO 2004035057 A1 UPAB: 20060203
NOVELTY - A combination comprises an endothelin receptor antagonist (A1) or its salt and an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) (A2) or its salt. ACTIVITY - Cytostatic.
MECHANISM OF ACTION - Endothelin receptor antagonist; Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI); Cancer cell proliferation inhibitor.
Test details are described, but no specific results are given.
USE - The combination is useful in the manufacture of a medicament for the treatment of cancer e.g. esophageal cancer, myeloma, hepatocellular, pancreatic, cervical cancer, Ewing's tumor, neuroblastoma, Kaposi's sarcoma, ovarian cancer, breast cancer, colorectal cancer, prostate cancer, bladder cancer, melanoma, lung cancer-non small cell lung cancer, small cell lung cancer, gastric cancer, head and neck cancer, brain cancer, renal cancer, lymphoma, cancer that is producing bone metastases and a non-metastatic state and leukemia and in the production of an anti-angiogenic effect in a warm-blooded animal (claimed).
ADVANTAGE - The combination provides synergistic and/or additive effect in the treatment of cancer. MANUAL CODE: CPI: B04-C01A; B04-N04A; B06-A01; B06-A02; B06-D01;
B06-D03; B06-D06; B06-D08; B07-D04C; B07-D10; B07-D12; B07-D13; B07-E01; B07-E04; B14-D06; B14-F02; B14-H01;

B14-L06; B14-S09

L12 ANSWER 17 OF 39 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-348130 [32] WPIX
DOC. NO. CPI: C2004-132455 [32]
TITLE: Composition useful for the treatment or prevention of headache that results from administration of endothelial antagonist comprises 5-hydroxytryptamine subtype receptor agonist
DERWENT CLASS: B05
INVENTOR: CURWEN J O; HUGHES A M; JOHNSTONE D; MORRIS C D
PATENT ASSIGNEE: (ASTR-C) ASTRAZENECA AB; (ASTR-C) ASTRAZENECA UK LTD
COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004032922	A1	20040422	(200432)*	EN	25[0]	A61K031-4045
AU 2003274307	A1	20040504	(200465)	EN		
EP 1551395	A1	20050713	(200546)	EN		
US 20060009512	A1	20060112	(200605)	EN		
JP 2006508933	W	20060316	(200620)	JA	19	
TW 2004016031	A	20040901	(200624)	ZH		A61K031-4045

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004032922	A1	WO 2003-GB4338	20031006
AU 2003274307	A1	AU 2003-274307	20031006
EP 1551395	A1	EP 2003-758297	20031006
EP 1551395	A1	WO 2003-GB4338	20031006
US 20060009512	A1	WO 2003-GB4338	20031006
JP 2006508933	W	WO 2003-GB4338	20031006
JP 2006508933	W	JP 2004-542622	20031006
US 20060009512	A1	US 2005-530232	20050404
TW 2004016031	A	TW 2003-128114	20031009

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003274307	A1	Based on	WO 2004032922	A
EP 1551395	A1	Based on	WO 2004032922	A
JP 2006508933	W	Based on	WO 2004032922	A

PRIORITY APPLN. INFO: GB 2002-23367 20021009
INT. PATENT CLASSIF.:
MAIN: A61K031-4045
SECONDARY: A61K031-18; A61K031-192; A61K031-216; A61K031-404; A61K031-405; A61K031-422; A61K031-445; A61K031-48; A61K031-506; A61K031-635; A61P025-06
IPC ORIGINAL: A61K0031-403 [I,C]; A61K0031-405 [I,A]; C07D0209-00 [I,C] ; C07D0209-18 [I,A]; A61K0031-422 [I,A]; A61K0031-4965 [I,C]; A61K0031-497 [I,A]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61K0045-06 [I,A]; A61P0025-00 [I,C]; A61P0025-04 [I,A]; A61P0029-00 [I,A]; A61P0035-00 [I,A]; A61P0035-02 [I,A]; A61P0043-00 [I,A]

BASIC ABSTRACT:

WO 2004032922 A1 UPAB: 20060121
NOVELTY - A composition comprises 5-hydroxytryptamine-1B/1D (5-HT-1B/1D) receptor agonist (A) or their salt in association with diluent or carrier.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a combination comprising an endothelin receptor antagonist (B) and (A) or their salt.
ACTIVITY - Analgesic; Cytostatic; Anti-HIV; Cardiovascular-Gen.; Hypotension; Cardiant; Antilipemic; Antiarteriosclerotic; Vasotropic; Nephrotropic; Cerebroprotective; Hemostatic; Antiasthmatic; Gynecological; Tocolytic; Antianginal; Antidiabetic; Dermatological; Antiinflammatory; Respiratory-Gen.; Hepatotropic; Osteopathic; Antiulcer; Uropathic; Antimigraine; Ophthalmological; Antiarthritic; Antirheumatic; Antiangiogenic.
MECHANISM OF ACTION - 5-HT-1B/1D Receptor Agonist; Endothelin Receptor Antagonist.
USE - (A) is used for the manufacture of a medicament for the treatment or prevention of headache that results from administration of endothelial antagonist (B) in a warm blooded animals (preferably man). The composition of (A) and (B) is used in the treatment of cancer (e.g. oesophageal cancer, myeloma, hepatocellular, pancreatic, cervical cancer, ewings tumor, neuroblastoma, Kaposi's sarcoma, ovarian cancer, breast cancer, colorectal cancer, prostate cancer, metastatic or non-metastatic cancer, bladder cancer, melanoma, lung cancer, non small cell lung cancer, small cell lung cancer, gastric cancer, head or neck cancer, renal cancer lymphoma and leukemia) and cancer producing bone metastases; and for the production of an antiangiogenic effect (all claimed). For the treatment of cardiovascular diseases or medical conditions e.g. hypertension, pulmonary hypertension, congestive heart failure, dyslipidaemia, atherosclerosis, restenosis, acute and chronic renal failure, ischemic stroke, subarachnoid hemorrhage, intermittent claudication, critical limb ischemia, asthma, organ failure after general surgery or transplantation, pre-eclampsia, premature labor, myocardial infarction, angina pectoris, dysarrhythmia, cardiogenic and endotoxin shock, diabetes mellitus, Raynaud's disease, scleroderma, Buerger's disease, systemic sclerosis, bronchitis, acute respiratory distress syndrome, liver cirrhosis, osteoporosis, Crohn's disease, ulcerative colitis, irritable bowel syndrome, urinary incontinence, migraine, glaucoma and arthritis (such as rheumatoid arthritis and osteoarthritis).
ADVANTAGE - The 5HT-1B/1D receptors mediate cerbrovascular vasoconstriction and inhibit neurogenic inflammation. MANUAL CODE: CPI: B04-C01A; B04-C01B; B04-N04A; B06-A02; B06-D01;
B06-D13; B07-D04C; B07-D10; B07-D12; B07-D13; B07-E01; B14-C01; B14-C09; B14-D01C; B14-E08; B14-E10C; B14-F01; B14-F02; B14-F06; B14-F07; B14-F08; B14-G02C; B14-H01; B14-J03; B14-K01; B14-L06; B14-M01; B14-N01; B14-N03; B14-N07D; B14-N10; B14-N12; B14-N14; B14-N16; B14-N17; B14-P03; B14-S01; B14-S04; B14-S06

L12 ANSWER 18 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6

ACCESSION NUMBER: 2000:311383 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000311383
TITLE: Zeneca ZD4054, an orally active endothelin-A receptor antagonist, prevents chronic hypoxia-induced pulmonary hypertension in the rat.
AUTHOR(S): Bialecki, R. [Reprint author]; Abbott, B. [Reprint author]; Barthlow, H. [Reprint author]; Caccese, R. [Reprint author]; Stow, R. [Reprint author]; Rumsey, W. [Reprint author]; Wilson, C.
CORPORATE SOURCE: Bioscience Department, Wilmington, DE, USA

SOURCE: FASEB Journal, (March 15, 2000) Vol. 14, No. 4, pp. A124. print.
Meeting Info.: Annual Meeting of Professional Research Scientists: Experimental Biology 2000. San Diego, California, USA. April 15-18, 2000. Federation of American Societies for Experimental Biology.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jul 2000
Last Updated on STN: 7 Jan 2002
CONCEPT CODE: Respiratory system - General and methods 16001
Biochemistry studies - General 10060
Biophysics - General 10502
Endocrine - General 17002
Pharmacology - General 22002
Cardiovascular system - General and methods 14501
General biology - Symposia, transactions and proceedings 00520
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology; Respiratory System (Respiration); Cardiovascular System (Transport and Circulation)
INDEX TERMS: Diseases
pulmonary hypertension: vascular disease, chronic hypoxia-induced
Hypertension, Pulmonary (MeSH)
INDEX TERMS: Chemicals & Biochemicals
ZD4054: Zeneca, endothelin type A receptor antagonist, orally active
INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L12 ANSWER 19 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:584881 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600595507
TITLE: Combined targeting of the endothelin A receptor and the epidermal growth factor receptor in ovarian cancer shows enhanced antiproliferative effects.
AUTHOR(S): Rosano, Laura [Reprint Author]; Di Castro, Valeriana; Spinella, Francesca; Natali, Pier Giorgio; Bagnato, Anna
CORPORATE SOURCE: Regina Elena Inst Canc Res, Mol Pathol Lab, Rome, Italy
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (APR 2006) Vol. 47, pp. 356.
Meeting Info.: 97th Annual Meeting of the American-Association-for-Cancer-Research (AACR). Washington, DC, USA. April 01 -05, 2006. Amer Assoc Canc Res.
ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2006
Last Updated on STN: 8 Nov 2006
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Reproductive system - Physiology and biochemistry 16504
Reproductive system - Pathology 16506
Endocrine - General 17002
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Therapeutic agents and therapy 24008
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology; Tumor Biology; Reproductive System (Reproduction)
INDEX TERMS: Diseases
ovarian cancer: neoplastic disease, reproductive system disease/female
Ovarian Neoplasms (MeSH)
INDEX TERMS: Chemicals & Biochemicals
endothelin-1 [ET-1]; epidermal growth factor receptor [EGFR]; endothelin A receptor; gefitinib [Iressa]: antineoplastic-drug, enzyme inhibitor-drug; p44/p42 mitogen-activated protein kinase [p44/p42 MAPK] [EC 2.7.1.37]; ZD4054: antineoplastic-drug
INDEX TERMS: Methods & Equipment
combination drug therapy: therapeutic and prophylactic techniques; monotherapy: therapeutic and prophylactic techniques, clinical techniques
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HEY cell line (cell_line): human ovarian carcinoma cells
OVCA 433 cell line (cell_line): human ovarian carcinoma cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
REGISTRY NUMBER: 123626-67-5 (endothelin-1)
123626-67-5 (ET-1)

184475-35-2 (gefitinib)
184475-35-2 (Iressa)

L12 ANSWER 20 OF 39 Elsevier BIOBASE COPYRIGHT 2007 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2006317686 ESBIOBASE Full-text
TITLE: Targeting bone metastasis in prostate cancer with endothelin receptor antagonists
AUTHOR: Carducci M.A.; Jimeno A.
CORPORATE SOURCE: M.A. Carducci, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Bunting-Blaustein Cancer Research Building, 1650 Orleans Street, Baltimore, MD 21231-1000, United States.
E-mail: carducci@jhmi.edu
SOURCE: Clinical Cancer Research, (15 OCT 2006), 12/20 PART 2 (6296s-6300s), 44 reference(s)
CODEN: CCREF4 ISSN: 1078-0432
DOCUMENT TYPE: Journal; General Review
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: Recent advances in the understanding of prostate cancer biology and its progression to bone metastasis have led to the development of drugs directed against precise molecular alterations in the prostate tumor cell and host cells in the normal bone environment such as osteoclasts and osteoblasts. Endothelins (ETs) and their receptors have emerged as a potential target in prostate cancer bone metastasis. By activating the ET.sub.A receptor, ET-1 is pathogenically involved in facilitating several aspects of prostate cancer progression, including proliferation, escape from apoptosis, invasion, and new bone formation, processes that are general to many malignancies. Notwithstanding, there are a number of features specifically driven by the ET axis in prostate cancer, such as creating and perpetuating a unique interaction between the metastatic prostate cancer cell and the bone microenvironment (osteoblast, osteoclast, and stroma) or altering the equilibrium in pain modulation. These features have led to the preferential clinical evaluation of atrasentan (ABT-627) as a biological therapy in prostate carcinoma, first in hormone-refractory prostate cancer. Biological activity of atrasentan in patients with prostate cancer has been shown by the suppression of biochemical markers of prostate cancer progression in bone, and clinical activity is evidenced by a consistent trend demonstrating a delay in time to disease progression when compared with placebo, especially in patients with bone metastases. Further studies of atrasentan and other selective ET-1 antagonists (ZD4054) are ongoing. .COPYRGT. 2006 American Association for Cancer Research.
CLASSIFICATION CODE: 87.2.2.2 CANCER RESEARCH: TUMOUR BIOLOGY: Cell Growth Control: Growth factors and inhibitors
87.5.16 CANCER RESEARCH: CLINICAL INVESTIGATIONS BY ORGAN SITE: Prostate
87.5.9.1 CANCER RESEARCH: CLINICAL INVESTIGATIONS BY ORGAN SITE: Bone and Soft Tissues: Bone, cartilage

L12 ANSWER 21 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006383733 EMBASE Full-text
TITLE: New molecular targets in advanced prostate cancer.
AUTHOR: Dawson N.A.
CORPORATE SOURCE: Dr. N.A. Dawson, Department of Medicine, Marlene and Stewart Greenebaum Cancer Center, University of Maryland, 22 South Greene Street, Baltimore, MD 21201-1595, United States. ndawson@umm.edu
SOURCE: Expert Review of Anticancer Therapy, (2006) Vol. 6, No. 7, pp. 993-1002. .

Refs: 98
ISSN: 1473-7140 E-ISSN: 1744-8328 CODEN: ERATBJ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Aug 2006
Last Updated on STN: 31 Aug 2006

ABSTRACT: Classically, advanced prostate cancer has been treated with hormonal therapy and, most recently, chemotherapy. This treatment clearly demonstrated a survival benefit, but never a cure. With the ever-expanding understanding of the pathophysiology of prostate cancer, there has been a recent explosion in the potential molecular targets and novel therapeutic approaches to both advanced and potentially localized prostate cancer. This review will focus on what the author perceives to be the most promising of these new strategies. The endothelin pathway has been identified as pivotal in the viscous cycle of tumorigenesis in bone, leading to the development of endothelial receptor antagonists. Vaccine therapy using autologous granulocyte-macrophage colony-stimulating factor-producing prostate cancer cells has been effective in producing both immune and clinical responses. Randomized clinical trials of the immunotherapy cell product APC8015 (Provenge®) have demonstrated improved survival in the hormone-refractory setting. The development of antisense oligonucleotides to segments of mRNA critical to the progression to androgen-independent disease has emerged as one further tool in the expanding armamentarium of potential therapies being tested. Clearly, headway is being made in improving outcomes in this most prevalent health problem. .COPYRGT. 2006 Future Drugs Ltd.

CONTROLLED TERM: Medical Descriptors:
*prostate cancer: DT, drug therapy
advanced cancer
drug targeting
cancer hormone therapy
cancer chemotherapy
cancer survival
pathophysiology
carcinogenesis
vaccination
cancer cell
immune response
drug response
immunotherapy
outcome assessment
gene therapy
peripheral edema: SI, side effect
rhinitis: SI, side effect
headache: SI, side effect
xerostomia: SI, side effect
dyspnea: SI, side effect
drug potentiation
oncolytic virus
Adenovirus
dendritic cell
bone marrow suppression: SI, side effect
human
nonhuman

clinical trial
review
CONTROLLED TERM: Drug Descriptors:
endothelin: EC, endogenous compound
endothelin receptor antagonist: CT, clinical trial
endothelin receptor antagonist: DT, drug therapy
endothelin receptor antagonist: PD, pharmacology
endothelin receptor antagonist: PO, oral drug administration
zd 4054: CT, clinical trial
zd 4054: DT, drug therapy
zd 4054: PD, pharmacology
zd 4054: PO, oral drug administration
granulocyte macrophage colony stimulating factor: CT, clinical trial
granulocyte macrophage colony stimulating factor: CM, drug comparison
granulocyte macrophage colony stimulating factor: DT, drug therapy
granulocyte macrophage colony stimulating factor: PD, pharmacology
provenge: CT, clinical trial
provenge: DT, drug therapy
antisense oligonucleotide: CT, clinical trial
antisense oligonucleotide: DT, drug therapy
antisense oligonucleotide: PD, pharmacology
antisense oligonucleotide: IV, intravenous drug administration
ogx 001: CT, clinical trial
ogx 001: DT, drug therapy
ogx 001: PD, pharmacology
ogx 001: IV, intravenous drug administration
messenger RNA
gonadorelin agonist: DT, drug therapy
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: CM, drug comparison
docetaxel: DT, drug therapy
prednisone: CT, clinical trial
prednisone: CB, drug combination
prednisone: CM, drug comparison
prednisone: DT, drug therapy
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: CM, drug comparison
mitoxantrone: DT, drug therapy
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
atrasentan: AE, adverse drug reaction
atrasentan: CT, clinical trial
atrasentan: DT, drug therapy
atrasentan: PD, pharmacology
placebo
recombinant DNA
thymidine kinase: CT, clinical trial
thymidine kinase: AD, drug administration
thymidine kinase: CB, drug combination
thymidine kinase: DT, drug therapy
ganciclovir: CT, clinical trial
ganciclovir: CB, drug combination

ganciclovir: DT, drug therapy
ganciclovir: IV, intravenous drug administration
cytosine deaminase: CT, clinical trial
cytosine deaminase: DT, drug therapy
cytosine deaminase: PD, pharmacology
fluorouracil
antineoplastic agent: AD, drug administration
antineoplastic agent: IT, drug interaction
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
cv 706: AD, drug administration
cv 706: IT, drug interaction
cv 706: DT, drug therapy
cv 706: PD, pharmacology
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
protein p53: CT, clinical trial
protein p53: AD, drug administration
cancer vaccine: CT, clinical trial
cancer vaccine: DT, drug therapy
prostate specific membrane antigen
antibody: AE, adverse drug reaction
antibody: CT, clinical trial
antibody: CB, drug combination
antibody: DT, drug therapy
lutetium 177: AE, adverse drug reaction
lutetium 177: CT, clinical trial
lutetium 177: CB, drug combination
lutetium 177: DT, drug therapy
17 allylamino 17 demethoxygeldanamycin: CT, clinical trial
17 allylamino 17 demethoxygeldanamycin: DT, drug therapy
17 allylamino 17 demethoxygeldanamycin: PD, pharmacology
unindexed drug
unclassified drug
gvax

CAS REGISTRY NO.: (docetaxel) 114977-28-5; (prednisone) 53-03-2; (mitoxantrone) 65271-80-9, 70476-82-3; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (thymidine kinase) 9002-06-6, 9086-73-1; (ganciclovir) 82410-32-0; (cytosine deaminase) 9025-05-2; (fluorouracil) 51-21-8; (paclitaxel) 33069-62-4; (lutetium 177) 14265-75-9

CHEMICAL NAME: (1) Apc 8015; (2) Gvax; (3) Provenge; (4) Ogx 001; Xinlay; Zd 4054; Cv 706

COMPANY NAME: (2) Cell Genesys; (3) Dendreon; (4) Oncogenex

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ACCESSION NUMBER: 2006342027 EMBASE Full-text

TITLE: New Targets in the Management of Prostate Cancer.

AUTHOR: Heath E.I.; Carducci M.A.

CORPORATE SOURCE: Dr. E.I. Heath, Barbara Ann Karmanos Cancer Institute, 4100 John R, 4 HWCRC, Detroit, MI 48201, United States. heathe@karmanos.org

SOURCE: Hematology/Oncology Clinics of North America, (2006) Vol. 20, No. 4, pp. 985-999.
Refs: 79
ISSN: 0889-8588 CODEN: HCNAEQ

PUBLISHER IDENT.: S 0889-8588(06)00106-7

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Aug 2006
Last Updated on STN: 10 Aug 2006

ABSTRACT: Our understanding of growth factors and growth-factor receptors, signal transduction pathways, cellular survival pathways, angiogenesis, and their potential roles in prostate-cancer tumorigenesis remains a work in progress. Novel agents targeting these key mechanisms are showing promise in clinical trials. Many more agents, including those not discussed in this article, such as radiopharmaceuticals, bisphosphonates, nutriceuticals, immunotherapy, and newer generation chemotherapy, are also showing promise as emerging treatments for prostate cancer. It is important to recognize when designing clinical trials of novel agents that traditional endpoints of disease response may not be applicable in measuring success of biologic compounds. Especially in a disease where tumor marker levels are critical for both patient and physician, additional biomarkers are necessary to better assess response. Halting drug development due to lack of response in serum PSA may lead to an unnecessary demise of an active agent. As expected, the combination of biologic agent with cytotoxic chemotherapy has a higher traditional response rate compared with biologic agent alone. The challenge of combination trials is to determine if the combination of agents will produce a higher traditional response rate compared with chemotherapy alone. For several of the agents discussed, the clinical benefit derived from a combination of biologic agent and cytotoxic chemotherapy may not justify additional drug toxicity. Efficient trial design, appropriate selection of correlative markers, and close toxicity monitoring will help improve our ability to identify promising novel agents.

CONTROLLED TERM: Medical Descriptors:
*prostate cancer: DT, drug therapy
cancer combination chemotherapy
target cell destruction
signal transduction
angiogenesis
food and drug administration
antineoplastic activity
breast metastasis: CO, complication
breast metastasis: DT, drug therapy
colorectal cancer: DT, drug therapy
drug efficacy
advanced cancer
cancer screening
fluorescence in situ hybridization
gene overexpression
pancreas islet cell carcinoma: DT, drug therapy
overall survival
cancer survival
survival rate
survival time
lung cancer: DT, drug therapy
drug cytotoxicity: SI, side effect
pulmonary hypertension: DT, drug therapy
QT prolongation: SI, side effect
kidney carcinoma: DT, drug therapy
kidney metastasis: DT, drug therapy
kidney graft rejection: DT, drug therapy

kidney graft rejection: PC, prevention
graft recipient
cell survival
DNA binding
gene control
epigenetics
DNA methylation
morning sickness: DT, drug therapy
teratogenicity: SI, side effect
pregnant woman
cardiotoxicity: SI, side effect
neurotoxicity: SI, side effect
gastrointestinal toxicity: SI, side effect
human
clinical trial
review
priority journal

CONTROLLED TERM: Drug Descriptors:
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: DT, drug therapy
panitumumab: DT, drug therapy
panitumumab: IV, intravenous drug administration
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: DT, drug therapy
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy
trastuzumab: IV, intravenous drug administration
matuzumab: CT, clinical trial
matuzumab: DT, drug therapy
paclitaxel: CB, drug combination
paclitaxel: DT, drug therapy
paclitaxel: IV, intravenous drug administration
estramustine: CT, clinical trial
estramustine: CB, drug combination
estramustine: DT, drug therapy
pertuzumab: CT, clinical trial
pertuzumab: DT, drug therapy
pertuzumab: IV, intravenous drug administration
gefitinib: CT, clinical trial
gefitinib: CB, drug combination
gefitinib: DT, drug therapy
gefitinib: PO, oral drug administration
erlotinib: CT, clinical trial
erlotinib: CB, drug combination
erlotinib: DT, drug therapy
erlotinib: PO, oral drug administration
6 (4 hydroxyphenyl) 4 (alpha methylbenzylamino) 7h pyrrolo[2,3 d]pyrimidine: DT, drug therapy
lapatinib: DT, drug therapy
pelitinib: DT, drug therapy
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6 quinazolinyl]acrylamide: DT, drug therapy
n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6 quinazolinyl]acrylamide: PO, oral drug administration
imatinib: AE, adverse drug reaction
imatinib: CT, clinical trial
imatinib: CB, drug combination

imatinib: DT, drug therapy
leflunomide: DT, drug therapy
zoledronic acid: CT, clinical trial
zoledronic acid: CB, drug combination
zoledronic acid: DT, drug therapy
atrasentan: CT, clinical trial
atrasentan: DT, drug therapy
bosentan: DT, drug therapy
bosentan: PO, oral drug administration
zd 4054: CT, clinical trial
zd 4054: DT, drug therapy
protein farnesyltransferase inhibitor: AE, adverse drug reaction
protein farnesyltransferase inhibitor: CT, clinical trial
protein farnesyltransferase inhibitor: DT, drug therapy
protein farnesyltransferase inhibitor: PO, oral drug administration
l 778123: AE, adverse drug reaction
l 778123: CT, clinical trial
l 778123: DT, drug therapy
tipifarnib: CT, clinical trial
tipifarnib: DT, drug therapy
tipifarnib: PO, oral drug administration
lonafarnib: CT, clinical trial
lonafarnib: DT, drug therapy
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: CT, clinical trial
3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine: DT, drug therapy
sorafenib: DT, drug therapy
sorafenib: PO, oral drug administration
rapamycin: CT, clinical trial
rapamycin: DT, drug therapy
temsirolimus: CT, clinical trial
temsirolimus: DT, drug therapy
ap 23573: CT, clinical trial
ap 23573: DT, drug therapy
unindexed drug
unclassified drug
everolimus
bortezomib
cep 7055
lenalidomide
serine 2 methoxy 5 [2 (3,4,5 trimethoxyphenyl)vinyl]anilide azd 2171
vandetanib
n acetylcolchinol phosphate
sunitinib
semaxanib
vatalanib
3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide

CAS REGISTRY NO.: (cetuximab) 205923-56-4; (panitumumab) 339177-26-3; (docetaxel) 114977-28-5; (trastuzumab) 180288-69-1; (matuzumab) 339186-68-4; (paclitaxel) 33069-62-4; (estramustine) 2998-57-4, 62899-40-5; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (erlotinib) 183319-69-9, 183321-74-6; (lapatinib) 388082-78-8,

437755-78-7; (pelitinib) 257933-82-7; (n [4 (3 chloro 4 fluoroanilino) 7 (3 morpholinopropoxy) 6 quinazolinyl]acrylamide) 267243-28-7, 338796-35-3; (imatinib) 152459-95-5, 220127-57-1; (leflunomide) 75706-12-6; (zoledronic acid) 118072-93-8, 131654-46-1, 165800-06-6, 165800-07-7; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (bosentan) 147536-97-8, 157212-55-0; (tipifarnib) 192185-72-1; (lonafarnib) 193275-84-2; (3 benzyl 7 cyano 2,3,4,5 tetrahydro 1 (1h imidazol 4 ylmethyl) 4 (2 thienylsulfonyl) 1h 1,4 benzodiazepine) 195981-08-9, 195987-41-8; (sorafenib) 284461-73-0; (rapamycin) 53123-88-9; (temsirolimus) 162635-04-3, 343261-52-9; (everolimus) 159351-69-6; (bortezomib) 179324-69-7, 197730-97-5; (lenalidomide) 191732-72-6; (serine 2 methoxy 5 [2 (3,4,5 trimethoxyphenyl)vinyl]anilide) 253426-24-3, 253609-44-8; (vandetanib) 338992-00-0, 338992-48-6, 443913-73-3; (n acetylcolchinol phosphate) 219923-05-4; (sunitinib) 341031-54-7, 557795-19-4; (semaxanib) 186610-95-7; (vatalanib) 212141-54-3, 212142-18-2; (3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide) 443912-23-0

CHEMICAL NAME: (1) Erbitux; (2) Emd 72000; (3) Omnitarg; (4) Iressa; (5) Pki 166; (6) Gw 572016; (7) Ekb 569; (8) Ci 1033; (9) Xinlay; (10) L 778123; (11) Zarnestra; (12) Sarasar; (13) Bms 214662; (14) Bay 439006; (15) Rapamune; (16) Rad001; (17) Ap 23573; (18) Velcade; (19) Cep 7055; (20) Cc 5013; (21) Ave 8062; Tarceva; Zd 4054; Azd 2171; Zd 6474; Zd 6126; Gleevec; Su 101; Su 011248; Su 5416; Cci 779; Ptk 787; Cc4047

COMPANY NAME: (1) Imclone (United States); (2) Emd pharmaceutical (United States); (3) Genentech; (4) Astra Zeneca (United Kingdom); (6) Glaxo SmithKline (United Kingdom); (8) Pfizer (United States); (9) Abbott (United States); (10) Merck (United States); (11) Johnson and Johnson (United States); (12) Schering Plough (United States); (13) Bristol (United States); (14) Bayer (Germany); (15) Wyeth (United States); (16) Novartis (Switzerland); (17) Ariad (United States); (18) Millennium (United States); (19) Cephalon (United States); (20) Celgene (United States); (21) Sanofi Aventis (France); Abgenix (United States); Kosan (United States); Medicis (United States); Methylgene (Canada); CuraGen (Denmark); Osi (United States); Waltham (United States); Antisoma (United Kingdom)

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ACCESSION NUMBER: 2006409130 EMBASE Full-text

TITLE: R&D technology investments: misguided and expensive or a better way to discover medicines?.

AUTHOR: Schmid E.F.; Smith D.A.

CORPORATE SOURCE: E.F. Schmid, Strategic Management Group, Sandwich Laboratories, Pfizer Global Research and Development, Sandwich, Kent CT13 9NJ, United Kingdom. esther.schmid@pfizer.com

SOURCE: Drug Discovery Today, (2006) Vol. 11, No. 17-18, pp. 775-784. .
Refs: 31
ISSN: 1359-6446 CODEN: DDTOFS

PUBLISHER IDENT.: S 1359-6446(06)00283-2

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer
037 Drug Literature Index
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 13 Sep 2006
Last Updated on STN: 13 Sep 2006

ABSTRACT: The pharmaceutical industry is in crisis owing to spiralling costs and a lack of new product launches. It is said that expensive investments in technology have not paid off. But is this really true? In this review, we explore some of the recent medicines that were, or are being, brought to market, and we discuss how they were discovered and what difference new technologies have made during the discovery of these medicines.

CONTROLLED TERM: Medical Descriptors:
food and drug administration
risk benefit analysis
high throughput screening
drug marketing
cancer therapy
breast cancer: DT, drug therapy
lung non small cell cancer: DT, drug therapy
colorectal cancer: DT, drug therapy
chronic myeloid leukemia: DT, drug therapy
kidney carcinoma: DT, drug therapy
nonhodgkin lymphoma: DT, drug therapy
acute lymphocytic leukemia: DT, drug therapy
multiple myeloma: DT, drug therapy
drug efficacy
melanoma: DT, drug therapy
endometrium cancer: DT, drug therapy
solid tumor: DT, drug therapy
Human immunodeficiency virus infection: DT, drug therapy
acquired immune deficiency syndrome: DT, drug therapy
atherosclerosis: DT, drug therapy
drug industry
human
nonhuman
clinical trial
meta analysis
systematic review
review

CONTROLLED TERM: Drug Descriptors:
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: AN, drug analysis
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DV, drug development
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PR, pharmaceutics
*antineoplastic agent: PD, pharmacology
imatinib: DT, drug therapy
imatinib: PD, pharmacology
sunitinib: DT, drug therapy
sunitinib: PD, pharmacology
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
tamoxifen citrate: DT, drug therapy
tamoxifen citrate: PD, pharmacology

exemestane: DT, drug therapy
exemestane: PD, pharmacology
erlotinib: DT, drug therapy
erlotinib: PD, pharmacology
cetuximab: DT, drug therapy
tositumomab i 131: DT, drug therapy
gefitinib: DT, drug therapy
sorafenib: DT, drug therapy
ibritumomab tiuxetan: DT, drug therapy
asparaginase: DT, drug therapy
bevacizumab: DT, drug therapy
bortezomib: DT, drug therapy
tipifarnib: CT, clinical trial
tipifarnib: DT, drug therapy
cp 675206: CT, clinical trial
cp 675206: DT, drug therapy
ispenesib: CT, clinical trial
ispenesib: DT, drug therapy
lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
n benzoylstaurosporine: CT, clinical trial
n benzoylstaurosporine: DT, drug therapy
everolimus: CT, clinical trial
everolimus: DT, drug therapy
alvocidip: CT, clinical trial
alvocidip: DT, drug therapy
n cyclohexyl n ethyl 3 (3 chloro 4 cyclohexylphenyl) 2 propenylamine: CT, clinical trial
n cyclohexyl n ethyl 3 (3 chloro 4 cyclohexylphenyl) 2 propenylamine: DT, drug therapy
meclinertant: CT, clinical trial
meclinertant: DT, drug therapy
pertuzumab: CT, clinical trial
pertuzumab: DT, drug therapy
zd 4054: CT, clinical trial
zd 4054: DT, drug therapy
vorinostat: CT, clinical trial
vorinostat: DT, drug therapy
maraviroc: CT, clinical trial
maraviroc: AN, drug analysis
maraviroc: DV, drug development
maraviroc: DT, drug therapy
maraviroc: PR, pharmaceutics
maraviroc: PD, pharmacology
torcetrapib: AN, drug analysis
torcetrapib: CB, drug combination
torcetrapib: DV, drug development
torcetrapib: DT, drug therapy
torcetrapib: PR, pharmaceutics
torcetrapib: PD, pharmacology
unindexed drug
unclassified drug
rofecoxib
nexavar
gemtuzumab ozogamicin
tykerb
uvidem
atorvastatin
pravastatin

CAS REGISTRY NO.: (imatinib) 152459-95-5, 220127-57-1; (sunitinib) 341031-54-7, 557795-19-4; (trastuzumab) 180288-69-1; (tamoxifen citrate) 54965-24-1; (exemestane) 107868-30-4; (erlotinib) 183319-69-9, 183321-74-6; (cetuximab) 205923-56-4; (tositumomab i 131) 192391-48-3; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (sorafenib) 284461-73-0; (ibritumomab tiuxetan) 206181-63-7; (asparaginase) 9015-68-3; (bevacizumab) 216974-75-3; (bortezomib) 179324-69-7, 197730-97-5; (tipifarnib) 192185-72-1; (lapatinib) 388082-78-8, 437755-78-7; (n benzoylstaurosporine) 120685-11-2; (everolimus) 159351-69-6; (maraviroc) 376348-65-1; (torcetrapib) 262352-17-0; (rofecoxib) 162011-90-7, 186912-82-3; (atorvastatin) 134523-00-5, 134523-03-8; (pravastatin) 81131-74-0

CHEMICAL NAME: (1) Vioxx; (2) Gleevec; (3) Sutent; (4) Herceptin; (5) Nolvadex; (6) Aromasin; (7) Tarceva; (8) Erbitux; (9) Bexxar; (10) Iressa; (11) Nexavar; (12) Zevalin; (13) Mylotarg; (14) Elspar; (15) Avastin; (16) Velcade; (17) Zarnestra; (18) Cp 675206; (19) Tykerb; (20) Pkc 412; (21) Rad 001; (22) Alvocidip; (23) Sr 31747; (24) Meclinertant; (25) Uvidem; (26) Omnitarg; (27) Zd 4054; (28) Vorinostat; (29) Lipitor; (30) Pravachol

COMPANY NAME: (7) Osi; (8) Imclone; (9) Corixa; (11) Bayer; (12) Idec; (13) Wyeth; (16) Millennium; (17) Johnson and Johnson; (19) Glaxo SmithKline; (21) Novartis; (25) Sanofi Aventis; (26) Genentech; (27) Astra Zeneca; (28) Merck; (29) Pfizer; (30) Bristol Myers Squibb

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ACCESSION NUMBER: 2006027795 EMBASE Full-text
TITLE: Annual update 2004/2005 - Treatment of genitourinary cancers.
AUTHOR: Hurtado P.
SOURCE: Drugs of the Future, (2005) Vol. 30, No. 9, pp. 975-980. Refs: 3
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Feb 2006
Last Updated on STN: 2 Feb 2006
CONTROLLED TERM: Medical Descriptors:
*urogenital tract cancer: DT, drug therapy
bladder cancer: DT, drug therapy
kidney cancer: DT, drug therapy
kidney carcinoma: DT, drug therapy
kidney metastasis: DT, drug therapy
penis cancer: DT, drug therapy
prostate cancer: DT, drug therapy
testis cancer: DT, drug therapy
human
clinical trial
review
Drug Descriptors:
bacterial DNA: CT, clinical trial
bacterial DNA: DT, drug therapy

lapatinib: CT, clinical trial
lapatinib: DT, drug therapy
vinflunine: CT, clinical trial
vinflunine: DT, drug therapy
carboplatin: CT, clinical trial
carboplatin: DT, drug therapy
mitomycin: CT, clinical trial
mitomycin: DT, drug therapy
celecoxib: CT, clinical trial
celecoxib: DT, drug therapy
pemetrexed: CT, clinical trial
pemetrexed: DT, drug therapy
irinotecan: CT, clinical trial
irinotecan: DT, drug therapy
genistein: CT, clinical trial
genistein: DT, drug therapy
gefitinib: CT, clinical trial
gefitinib: DT, drug therapy
17 allylamino 17 demethoxygeldanamycin: CT, clinical trial
17 allylamino 17 demethoxygeldanamycin: DT, drug therapy
ixabepilone: CT, clinical trial
ixabepilone: DT, drug therapy
gemcitabine: CT, clinical trial
gemcitabine: DT, drug therapy
Flt3 ligand: CT, clinical trial
Flt3 ligand: DT, drug therapy
dolastatin 10: CT, clinical trial
dolastatin 10: DT, drug therapy
recombinant interleukin 12
sunitinib: CT, clinical trial
sunitinib: DT, drug therapy
sorafenib: CT, clinical trial
sorafenib: DT, drug therapy
temsirolimus: CT, clinical trial
temsirolimus: DT, drug therapy
tegafur: CT, clinical trial
tegafur: DT, drug therapy
thalidomide: CT, clinical trial
thalidomide: DT, drug therapy
iboctadekin: CT, clinical trial
iboctadekin: DT, drug therapy
gadolinium texaphyrin: CT, clinical trial
gadolinium texaphyrin: DT, drug therapy
gti 2040: CT, clinical trial
gti 2040: DT, drug therapy
erlotinib: CT, clinical trial
erlotinib: DT, drug therapy
depsipeptide: CT, clinical trial
depsipeptide: DT, drug therapy
atrasentan: CT, clinical trial
atrasentan: DT, drug therapy
bevacizumab: CT, clinical trial
bevacizumab: DT, drug therapy
goserelin: CT, clinical trial
goserelin: DT, drug therapy
unindexed drug
cg 0070
amg 706
srl 172
zrx 101

ec 17
agro 100
mg 98
imo 2055
cp 461
idn 5109
cnto 328
mdx 010
provenge
dn 101
zd 4054
pi 88
ogx 011
5,6 dimethylxanthenone 4 acetic acid
mt 201
j 591
gti 2501
ctl 102
cm 31747
lenalidomide
ap 23573
mln 2704
sm 1531
gpi 0100
emd 273066
abr 215050
ssr 125329a
rc 8800
nbi 56418
nbi 42902
insm 18
pck 3145
mdx 070
gcan 101
3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide

CAS REGISTRY NO.: (lapatinib) 388082-78-8, 437755-78-7; (vinflunine) 162652-95-1; (carboplatin) 41575-94-4; (mitomycin) 1404-00-8; (celecoxib) 169590-42-5; (pemetrexed) 137281-23-3, 150399-23-8; (irinotecan) 100286-90-6; (genistein) 446-72-0; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (ixabepilone) 219989-84-1; (gemcitabine) 103882-84-4; (Flt3 ligand) 171404-15-2; (dolastatin 10) 110417-88-4; (sunitinib) 341031-54-7, 557795-19-4; (sorafenib) 284461-73-0; (temsirolimus) 162635-04-3, 343261-52-9; (tegafur) 17902-23-7; (thalidomide) 50-35-1; (iboctadekin) 479198-61-3; (gadolinium texaphyrin) 165254-24-0, 194083-75-5; (erlotinib) 183319-69-9, 183321-74-6; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (bevacizumab) 216974-75-3; (goserelin) 65807-02-5; (idn 5109) 186348-05-0, 186348-23-2; (lenalidomide) 191732-72-6; (3 (4 amino 1,3 dihydro 1,3 dioxo 2h isoindol 2 yl)glutarimide) 443912-23-0

CHEMICAL NAME: (1) Cg 0070; (2) Amg 706; (3) Srl 172; (4) Nsc 330507; (5) Zrx 101; (6) Ec 17; (7) Agro 100; (8) Sb 485232; (9) Mg 98; (10) Imo 2055; (11) Gti 2040; (12) Cp 461; (13) Bay 598862; (14) Cnto 328; (15) Mdx 010; (16) Apc 8015; (17) Dn 101; (18) Zd 4054; (19) Pi 88; (20) Ogx 011; (21) Nsc 640488; (22) Nsc 330507; (23) Mt 201; (24) J 591; (25) Gti 2501; (26) Ctl 102; (27) Cm 31747; (28) Cc 5013; (29) Ap

23573; (30) Mln 2704; (31) Sm 1531; (32) Gpi 0100; (33) Emd 273066; (34) Abr 215050; (35) Ssr 125329a; (36) Rc 8800; (37) Nbi 56418; (38) Nbi 42902; (39) Insm 18; (40) Pck 3145; (41) Mdx 070; (42) Gcan 101; (43) Cc 4047

COMPANY NAME: (1) Cell.Genesys; (2) Amgen; (3) SR Pharma; (5) Zellerx; (6) Endocyte; (8) Glaxo SmithKline; (9) MGI; (10) Hybridon; (12) Osi; (13) Bayer; (14) Centocor; (16) Dendreon; (18) National Cancer Institute (United States); (19) Progen; (20) Oncogenex; (21) Antisoma; (22) Kosan; (23) Micromet; (24) BZL Biologics; (25) Lorus; (26) Innovata Biomed; (29) Ariad; (30) Millennium; (31) Cytogen; (32) Galenica; (33) EMD Biosciences; (34) Active Biotech; (35) Sanofi Aventis; (36) Rejuvenon; (38) Neurocrine Biosciences; (39) Insmed; (40) Procyon; (41) Medarex; (42) Gammacan; (43) Calgene

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ACCESSION NUMBER: 2006019293 EMBASE Full-text

TITLE: Ambrisentan: Treatment of pulmonary arterial hypertension endothelin ET(A) receptor antagonist.

AUTHOR: Sorbera L.A.; Castaner J.

CORPORATE SOURCE: L.A. Sorbera, Prous Science, P.O. Box 540, 08080 Barcelona, Spain

SOURCE: Drugs of the Future, (2005) Vol. 30, No. 8, pp. 765-770. .
Refs: 58
ISSN: 0377-8282 CODEN: DRFUD4

COUNTRY: Spain

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 2 Feb 2006
Last Updated on STN: 2 Feb 2006

ABSTRACT: Pulmonary artery hypertension (PAH) is a group of rare and progressive lung disorders. Because of the low incidence of the disease, progress in the search for treatments for PAH has been slow. Conventional therapy for mild to moderate PAH consists of diuretics, calcium channel blockers and anticoagulants, while options for patients with moderate to severe PAH are more limited (prostacyclin infusion and balloon atrial septostomy). However, research efforts in this field have intensified with several novel agents currently under active development. One such agent is the pyrimidine-derived ambrisentan, an endothelin receptor antagonist that is highly selective for ET(A). As compared to nonselective endothelin receptor antagonists, ambrisentan displays enhanced efficacy, a low propensity to cause liver toxicity and adverse drug interactions, a high oral bioavailability and a half-life enabling once-daily dosing. The efficacy of ambrisentan was demonstrated in clinical trials in patients with WHO class II and III PAH and it is presently undergoing phase III development for the treatment of PAH.

CONTROLLED TERM: Medical Descriptors:
*pulmonary hypertension: DT, drug therapy
lung disease: DT, drug therapy
hypertension: DT, drug therapy
hypertension: PC, prevention
drug structure
drug synthesis

drug bioavailability
drug half life
drug mechanism
lung artery pressure
lung vascular resistance
lung capillary pressure
vasoconstriction
aorta
basilar artery
iliac artery
pulmonary artery
drug efficacy
dyspnea
lung function test
forced expiratory volume
exercise test
treatment outcome
liver toxicity: SI, side effect
drug safety
drug selectivity
drug receptor binding
binding affinity
human
nonhuman
rat
major clinical study
clinical trial
phase 1 clinical trial
phase 2 clinical trial
phase 3 clinical trial
randomized controlled trial
double blind procedure
multicenter study
animal experiment
animal model
controlled study
animal tissue
animal cell
adult
article

CONTROLLED TERM: Drug Descriptors:
*ambrisentan: AE, adverse drug reaction
*ambrisentan: CT, clinical trial
*ambrisentan: AD, drug administration
*ambrisentan: AN, drug analysis
*ambrisentan: CM, drug comparison
*ambrisentan: DV, drug development
*ambrisentan: DO, drug dose
*ambrisentan: DT, drug therapy
*ambrisentan: PK, pharmacokinetics
*ambrisentan: PD, pharmacology
*ambrisentan: PO, oral drug administration
*endothelin A receptor antagonist: AE, adverse drug reaction
*endothelin A receptor antagonist: CT, clinical trial
*endothelin A receptor antagonist: AD, drug administration
*endothelin A receptor antagonist: AN, drug analysis
*endothelin A receptor antagonist: CM, drug comparison
*endothelin A receptor antagonist: DV, drug development
*endothelin A receptor antagonist: DO, drug dose

*endothelin A receptor antagonist: DT, drug therapy
*endothelin A receptor antagonist: PK, pharmacokinetics
*endothelin A receptor antagonist: PD, pharmacology
*endothelin A receptor antagonist: PO, oral drug administration
vasodilator agent: AE, adverse drug reaction
vasodilator agent: CT, clinical trial
vasodilator agent: AD, drug administration
vasodilator agent: AN, drug analysis
vasodilator agent: CM, drug comparison
vasodilator agent: DV, drug development
vasodilator agent: DO, drug dose
vasodilator agent: DT, drug therapy
vasodilator agent: PK, pharmacokinetics
vasodilator agent: PD, pharmacology
vasodilator agent: PO, oral drug administration
diuretic agent: DT, drug therapy
calcium channel blocking agent: DO, drug dose
calcium channel blocking agent: DT, drug therapy
nifedipine: DO, drug dose
nifedipine: DT, drug therapy
diltiazem: DO, drug dose
diltiazem: DT, drug therapy
anticoagulant agent: DT, drug therapy
anticoagulant agent: PO, oral drug administration
prostacyclin: DT, drug therapy
prostacyclin: IV, intravenous drug administration
sildenafil: DT, drug therapy
sildenafil: PD, pharmacology
sitaxsentan: CM, drug comparison
sitaxsentan: DV, drug development
sitaxsentan: PD, pharmacology
vasoactive intestinal polypeptide: CT, clinical trial
vasoactive intestinal polypeptide: DT, drug therapy
vasoactive intestinal polypeptide: PD, pharmacology
phosphodiesterase V inhibitor: CT, clinical trial
phosphodiesterase V inhibitor: DT, drug therapy
phosphodiesterase V inhibitor: PD, pharmacology
uk 369003: CT, clinical trial
uk 369003: DT, drug therapy
uk 369003: PD, pharmacology
serotonin 2B receptor
serotonin 2 antagonist: CT, clinical trial
serotonin 2 antagonist: DT, drug therapy
serotonin 2 antagonist: PD, pharmacology
prx 08066: CT, clinical trial
prx 08066: DT, drug therapy
prx 08066: PD, pharmacology
tbc 3711: CT, clinical trial
tbc 3711: CM, drug comparison
tbc 3711: DT, drug therapy
tbc 3711: PD, pharmacology
atrasentan: CM, drug comparison
atrasentan: PD, pharmacology
bosentan: CM, drug comparison
bosentan: PD, pharmacology
clazosentan: CM, drug comparison
clazosentan: PD, pharmacology
darusentan: CM, drug comparison
darusentan: PD, pharmacology

2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine 6 carboxylic acid: CM, drug comparison
2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine 6 carboxylic acid: PD, pharmacology
alpha [[1 butyl 5 [2 [(2 carboxyphenyl)methoxy] 4 methoxyphenyl] 1h pyrazol 4 yl]methylene] 6 methoxy 1,3 benzodioxole 5 propanoic acid: CM, drug comparison
alpha [[1 butyl 5 [2 [(2 carboxyphenyl)methoxy] 4 methoxyphenyl] 1h pyrazol 4 yl]methylene] 6 methoxy 1,3 benzodioxole 5 propanoic acid: PD, pharmacology
zd 4054: CM, drug comparison
zd 4054: PD, pharmacology
97 139: CM, drug comparison
97 139: PD, pharmacology
placebo
endothelin 1
endothelin A receptor
unclassified drug
lu 20807
prx 3711

CAS REGISTRY NO.: (ambrisentan) 177036-94-1; (nifedipine) 21829-25-4; (diltiazem) 33286-22-5, 42399-41-7; (prostacyclin) 35121-78-9, 61849-14-7; (sildenafil) 139755-83-2; (sitaxsentan) 184036-34-8, 210421-74-2; (vasoactive intestinal polypeptide) 37221-79-7; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (bosentan) 147536-97-8, 157212-55-0; (clazosentan) 180384-56-9; (darusentan) 171714-84-4; (2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine 6 carboxylic acid) 198279-45-7, 224448-58-2; (alpha [[1 butyl 5 [2 [(2 carboxyphenyl)methoxy] 4 methoxyphenyl] 1h pyrazol 4 yl]methylene] 6 methoxy 1,3 benzodioxole 5 propanoic acid) 209055-04-9
CHEMICAL NAME: (1) Bsf 208075; (2) Lu 20807; (3) Tbc 3711; (4) Prx 3711; (5) Uk 369003; (6) Thelin; (7) Revatio; (8) Aviptadil; 97 139; J 104132; Sb 234551; Zd 4054
COMPANY NAME: (2) Myogen (United States); (4) Predix; (6) Encysive; (7) Pfizer; (8) Mondobiotech

L12 ANSWER 26 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005578424 EMBASE Full-text
TITLE: Emerging role of the endothelin axis in ovarian tumor progression.
AUTHOR: Bagnato A.; Spinella F.; Rosano L.
CORPORATE SOURCE: A. Bagnato, Molecular Pathology and Ultrastructure Laboratory, Regina Elena Cancer Institute, Via delle Messi d'Oro 156, 00158 Rome, Italy. bagnato@ifo.it
SOURCE: Endocrine-Related Cancer, (2005) Vol. 12, No. 4, pp. 761-772. .
Refs: 73
ISSN: 1351-0088 CODEN: ERCAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2006
Last Updated on STN: 9 Feb 2006

ABSTRACT: Ovarian cancer is the leading cause of gynecologic cancer-related deaths. The endothelin (ET) axis, which includes ET-1, ET-2, ET-3, and the ET receptors, ET(A)R and ET(B)R, represents a novel target in tumor treatment. ET-1 may directly contribute to tumor growth and indirectly modulate tumor-host interactions in various tumors such as prostatic, ovarian, renal, pulmonary, colorectal, cervical, breast carcinoma, Kaposi's sarcoma, brain tumors and melanoma. Extensive experimental evidence links ET(A)R overexpression with tumor progression in ovarian cancer. ET(A)R engagement can in fact activate multiple signal transduction pathways including protein kinase C, phosphatidylinositol 3-kinase, mitogen-activated protein kinase and transactivate epidermal growth factor receptor, which play a role in ovarian tumor growth and invasion. The effects of ET(A)R signaling are wide ranging and involve both cancer cells and their surrounding stroma, including the vasculature. Upon being activated, the ET(A)R mediates multiple tumor-promoting activities, including enhanced cell proliferation, escape from apoptosis, angiogenesis, epithelial-mesenchymal transition and increased motility and invasiveness. These findings indicate that activation of ET(A)R by ET-1 is a key mechanism in the cellular signaling network promoting ovarian cancer growth and progression. The predominant role played by ET(A)R in cancer has led to the development of small molecules that antagonize the binding of ET-1 to ET(A)R. The emerging preclinical data presented here provide a rationale for the clinical evaluation of these molecules in which targeting the related signaling cascade via ET(A)R blockade may be advantageous in the treatment of advanced stage ovarian carcinoma. .COPYRGT. 2005 Society for Endocrinology Printed in Great Britain.

CONTROLLED TERM: Medical Descriptors:
*ovary tumor
*ovary cancer: EP, epidemiology
cancer growth
cancer mortality
gynecologic cancer: EP, epidemiology
prostate carcinoma
ovary carcinoma
kidney carcinoma
lung carcinoma
colorectal carcinoma
uterine cervix carcinoma
breast carcinoma
Kaposi sarcoma
brain tumor
melanoma
protein expression
signal transduction
cancer invasion
cancer cell
stroma
apoptosis
angiogenesis
epithelium
mesenchyme
cell motility
receptor binding
drug potency
regulatory mechanism
cancer chemotherapy

metastasis
cell communication
cell adhesion
drug bioavailability
drug tolerability
human
nonhuman
review
Drug Descriptors:
*endothelin 1
*endothelin 2
*endothelin 3
*endothelin A receptor
*endothelin B receptor
protein kinase C
phosphatidylinositol 3 kinase
mitogen activated protein kinase
epidermal growth factor receptor
endothelin A receptor antagonist: CB, drug combination
endothelin A receptor antagonist: DV, drug development
endothelin A receptor antagonist: IT, drug interaction
endothelin A receptor antagonist: PK, pharmacokinetics
endothelin A receptor antagonist: PD, pharmacology
atrasentan: CB, drug combination
atrasentan: IT, drug interaction
atrasentan: PK, pharmacokinetics
atrasentan: PD, pharmacology
zd 4054: DV, drug development
cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl): PD, pharmacology
antineoplastic agent: CB, drug combination
antineoplastic agent: IT, drug interaction
antineoplastic agent: PD, pharmacology
paclitaxel: CB, drug combination
paclitaxel: IT, drug interaction
paclitaxel: PD, pharmacology
endothelin B receptor antagonist: PD, pharmacology
n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine: PD, pharmacology
cyclooxygenase 1 inhibitor: PD, pharmacology
cyclooxygenase 2 inhibitor: PD, pharmacology
prostaglandin E receptor
prostaglandin receptor blocking agent: PD, pharmacology
cytotoxic agent
unclassified drug
ab 627

CAS REGISTRY NO.: (protein kinase C) 141436-78-4; (phosphatidylinositol 3 kinase) 115926-52-8; (mitogen activated protein kinase) 142243-02-5; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)) 136553-81-6; (paclitaxel) 33069-62-4; (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine) 156161-89-6
CHEMICAL NAME: Bq 123; Atrasentan; Zd 4054; Ab 627; Bq 788

L12 ANSWER 27 OF 39 EMBASE
ACCESSION NUMBER: 2005229986 EMBASE Full-text

TITLE: Novel therapies: Prostate cancer.
AUTHOR: Bryan J.
SOURCE: Pharmaceutical Journal, (7 May 2005) Vol. 274, No. 7348, pp. 555-556. .
Refs: 5
ISSN: 0031-6873 CODEN: PHJOAV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 2005
Last Updated on STN: 9 Jun 2005
CONTROLLED TERM: Medical Descriptors:
*prostate cancer: DT, drug therapy
*prostate cancer: RT, radiotherapy
*prostate cancer: SU, surgery
advanced cancer: DT, drug therapy
advanced cancer: RT, radiotherapy
advanced cancer: SU, surgery
cancer survival
drug approval
systematic review
licence
drug targeting
drug efficacy
drug safety
protein expression
cell proliferation
apoptosis
tumor vascularization
cancer combination chemotherapy
antineoplastic activity
drug response
drug selectivity
cancer adjuvant therapy
prostate surgery
treatment failure
human
nonhuman
male
clinical trial
meta analysis
article
Drug Descriptors:
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PD, pharmacology
atrasentan: CT, clinical trial
atrasentan: DT, drug therapy
gefitinib: DT, drug therapy
endothelin A receptor antagonist: CT, clinical trial
endothelin A receptor antagonist: DT, drug therapy
endothelin A receptor antagonist: PD, pharmacology
zd 4054: CT, clinical trial
zd 4054: DT, drug therapy

endothelin A receptor: EC, endogenous compound
endothelin B receptor: EC, endogenous compound
endothelin 1: EC, endogenous compound
vasculotropin: EC, endogenous compound
matrix metalloproteinase: EC, endogenous compound
integrin: EC, endogenous compound
bevacizumab: CT, clinical trial
bevacizumab: CB, drug combination
bevacizumab: DT, drug therapy
bevacizumab: PD, pharmacology
fluorouracil: CT, clinical trial
fluorouracil: CB, drug combination
fluorouracil: DT, drug therapy
thalidomide: CT, clinical trial
thalidomide: CB, drug combination
thalidomide: DT, drug therapy
thalidomide: PD, pharmacology
docetaxel: CT, clinical trial
docetaxel: CB, drug combination
docetaxel: CM, drug comparison
docetaxel: DT, drug therapy
cilengitide: CT, clinical trial
cilengitide: DT, drug therapy
cilengitide: PD, pharmacology
oblimersen: CT, clinical trial
oblimersen: CB, drug combination
oblimersen: CM, drug comparison
oblimersen: DT, drug therapy
oblimersen: PD, pharmacology
protein bcl 2: EC, endogenous compound
unclassified drug
CAS REGISTRY NO.: (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (vasculotropin) 127464-60-2; (bevacizumab) 216974-75-3; (fluorouracil) 51-21-8; (thalidomide) 50-35-1; (docetaxel) 114977-28-5; (cilengitide) 188968-51-6; (oblimersen) 190977-41-4; (protein bcl 2) 219306-68-0
CHEMICAL NAME: (1) Xinlay; (2) Zd 4054; (3) Avastin; Genasense
COMPANY NAME: (1) Abbott; (2) Astra Zeneca; (3) Genentech; EMD Pharmaceuticals (United States)

L12 ANSWER 28 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005294458 EMBASE Full-text
TITLE: American Society of Clinical Oncology - 41st Annual Meeting. Immunology. 13-17 May 2005, Orlando, FL, USA.
AUTHOR: Shah S.; Yager N.
CORPORATE SOURCE: S. Shah, Thomson Scientific, 34-42 Cleveland Street, London W1T 4JE, United Kingdom. saloni.shah@thomson.com
SOURCE: IDrugs, (2005) Vol. 8, No. 7, pp. 528-530. .
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English

ENTRY DATE: Entered STN: 21 Jul 2005
Last Updated on STN: 21 Jul 2005

CONTROLLED TERM: Medical Descriptors:
*tumor immunity
prostate cancer: DT, drug therapy
prostate cancer: SU, surgery
antineoplastic activity
cancer resistance
castration
cancer immunotherapy
drug structure
drug targeting
drug tolerability
metastasis: CO, complication
metastasis: DT, drug therapy
dose response
dyspnea: SI, side effect
peripheral edema: SI, side effect
headache: SI, side effect
brain hemorrhage: SI, side effect
maximum tolerated dose
fatigue: SI, side effect
nose congestion: SI, side effect
nausea: SI, side effect
alanine aminotransferase blood level
abnormal substrate concentration in blood: SI, side effect
drug dose reduction
neuropathy: SI, side effect
diarrhea: SI, side effect
optimal drug dose
tobacco dependence: DT, drug therapy
tobacco dependence: PC, prevention
immunogenicity
vaccination
flu like syndrome: SI, side effect
drug safety
drug efficacy
treatment failure
melanoma: DT, drug therapy
lung non small cell cancer: DT, drug therapy
neutropenia: SI, side effect
thrombocytopenia: SI, side effect
drug competition
vomiting: SI, side effect
blood toxicity: SI, side effect
abdominal pain: SI, side effect
pancreatitis: SI, side effect
treatment outcome
disease exacerbation
human
clinical trial
conference paper

CONTROLLED TERM: Drug Descriptors:
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: CT, clinical trial
antineoplastic agent: AN, drug analysis
antineoplastic agent: DO, drug dose
antineoplastic agent: IT, drug interaction
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology

antineoplastic agent: DL, intradermal drug administration
antineoplastic agent: IV, intravenous drug administration
antineoplastic agent: PO, oral drug administration
antineoplastic agent: SC, subcutaneous drug administration
zd 4054: AE, adverse drug reaction
zd 4054: CT, clinical trial
zd 4054: AN, drug analysis
zd 4054: DO, drug dose
zd 4054: DT, drug therapy
zd 4054: PD, pharmacology
zd 4054: PO, oral drug administration
antibody conjugate: AE, adverse drug reaction
antibody conjugate: CT, clinical trial
antibody conjugate: DO, drug dose
antibody conjugate: DT, drug therapy
antibody conjugate: IV, intravenous drug administration
mln 2704: AE, adverse drug reaction
mln 2704: CT, clinical trial
mln 2704: DO, drug dose
mln 2704: DT, drug therapy
mln 2704: IV, intravenous drug administration
mln 591
alanine aminotransferase: EC, endogenous compound
nicotine derivative: AE, adverse drug reaction
nicotine derivative: CT, clinical trial
nicotine derivative: DO, drug dose
nicotine derivative: DT, drug therapy
nicotine derivative: PK, pharmacokinetics
cyt 002: AE, adverse drug reaction
cyt 002: CT, clinical trial
cyt 002: DO, drug dose
cyt 002: DT, drug therapy
cyt 002: PK, pharmacokinetics
placebo
pertuzumab: AE, adverse drug reaction
pertuzumab: CT, clinical trial
pertuzumab: DO, drug dose
pertuzumab: DT, drug therapy
pertuzumab: IV, intravenous drug administration
taxane derivative: AE, adverse drug reaction
taxane derivative: CT, clinical trial
taxane derivative: CB, drug combination
taxane derivative: CM, drug comparison
taxane derivative: DT, drug therapy
platinum derivative: AE, adverse drug reaction
platinum derivative: CT, clinical trial
platinum derivative: CB, drug combination
platinum derivative: CM, drug comparison
platinum derivative: DO, drug dose
platinum derivative: DT, drug therapy
cpg 7909: AE, adverse drug reaction
cpg 7909: CT, clinical trial
cpg 7909: CB, drug combination
cpg 7909: CM, drug comparison
cpg 7909: DO, drug dose
cpg 7909: IT, drug interaction
cpg 7909: DT, drug therapy
cpg 7909: SC, subcutaneous drug administration
dacarbazine: AE, adverse drug reaction
dacarbazine: CT, clinical trial

dacarbazine: CB, drug combination
dacarbazine: CM, drug comparison
dacarbazine: DO, drug dose
dacarbazine: IT, drug interaction
dacarbazine: DT, drug therapy
dacarbazine: IV, intravenous drug administration
ing 1: AE, adverse drug reaction
ing 1: CT, clinical trial
ing 1: DO, drug dose
ing 1: DT, drug therapy
ing 1: IV, intravenous drug administration
ing 1: SC, subcutaneous drug administration
dendritic cell vaccine: AE, adverse drug reaction
dendritic cell vaccine: CT, clinical trial
dendritic cell vaccine: DT, drug therapy
dendritic cell vaccine: DL, intradermal drug administration
dendritic cell vaccine: SC, subcutaneous drug administration
unclassified drug
promune

CAS REGISTRY NO.: (alanine aminotransferase) 9000-86-6, 9014-30-6; (dacarbazine) 4342-03-4

CHEMICAL NAME: (1) Zd 4054; (2) Mln 2704; (3) Mln 2704; (4) Cyt 002; (5) Promune; (6) Cpg 7909; (7) Ing 1; Mln 591

COMPANY NAME: (1) Astra Zeneca; (2) Millennium Pharmaceuticals; (3) BZL Biologics; (4) Cytos biotechnology; (6) Pfizer; (7) Xoma; Genentech; Hoffmann La Roche; Chugai; ODC Therapy

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ACCESSION NUMBER: 2005254110 EMBASE Full-text

TITLE: Anticancer agents - Part II. 16-20 April 2005, Anaheim, CA, USA.

AUTHOR: Phillips T.; Collins T.; Davies J.

CORPORATE SOURCE: T. Phillips, Thomson Scientific, Middlesex Hse., 34-42 Cleveland St., London W1T 4JE, United Kingdom. tom.phillips@thomson.com

SOURCE: IDrugs, (2005) Vol. 8, No. 6, pp. 446-449. .
ISSN: 1369-7056 CODEN: IDRUFN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT:
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology

LANGUAGE: English

ENTRY DATE: Entered STN: 23 Jun 2005
Last Updated on STN: 23 Jun 2005

CONTROLLED TERM: Medical Descriptors:
lung non small cell cancer: DT, drug therapy
antineoplastic activity
dose response
single drug dose
drug efficacy
prostate cancer: DT, drug therapy
receptor blocking
drug structure
peripheral neuropathy: DT, drug therapy

peripheral neuropathy: PC, prevention
IC 50
drug selectivity
solid tumor: DT, drug therapy
area under the curve
drug half life
drug dose regimen
drug safety
melanoma: DT, drug therapy
drug potentiation
concentration response
bladder cancer: DT, drug therapy
drug targeting
vaccination
drug tolerability
nausea and vomiting: SI, side effect
oncolytic virus
human
nonhuman
clinical trial
conference paper

CONTROLLED TERM: Drug Descriptors:
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: AN, drug analysis
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DO, drug dose
*antineoplastic agent: IT, drug interaction
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: TO, drug toxicity
*antineoplastic agent: PK, pharmacokinetics
*antineoplastic agent: PD, pharmacology
*antineoplastic agent: IV, intravenous drug administration
*antineoplastic agent: PO, oral drug administration
recombinant protein: CT, clinical trial
recombinant protein: CB, drug combination
recombinant protein: CM, drug comparison
recombinant protein: DT, drug therapy
recombinant protein: PO, oral drug administration
talactoferrin alpha: CT, clinical trial
talactoferrin alpha: CB, drug combination
talactoferrin alpha: CM, drug comparison
talactoferrin alpha: DT, drug therapy
talactoferrin alpha: PO, oral drug administration
carboplatin: CT, clinical trial
carboplatin: CB, drug combination
carboplatin: CM, drug comparison
carboplatin: DT, drug therapy
paclitaxel: CT, clinical trial
paclitaxel: CB, drug combination
paclitaxel: CM, drug comparison
paclitaxel: DT, drug therapy
paclitaxel: TO, drug toxicity
prodrug: CT, clinical trial
prodrug: CM, drug comparison
prodrug: DO, drug dose
prodrug: DT, drug therapy
prodrug: TO, drug toxicity
prodrug: PD, pharmacology

dts 201: CT, clinical trial
dts 201: CM, drug comparison
dts 201: DO, drug dose
dts 201: DT, drug therapy
dts 201: TO, drug toxicity
dts 201: PD, pharmacology
doxorubicin: CM, drug comparison
doxorubicin: DO, drug dose
doxorubicin: DT, drug therapy
doxorubicin: TO, drug toxicity
doxorubicin: PD, pharmacology
endothelin A receptor antagonist: CT, clinical trial
endothelin A receptor antagonist: AN, drug analysis
endothelin A receptor antagonist: DO, drug dose
endothelin A receptor antagonist: DT, drug therapy
endothelin A receptor antagonist: PD, pharmacology
endothelin A receptor antagonist: PO, oral drug administration
zd 4054: CT, clinical trial
zd 4054: AN, drug analysis
zd 4054: DO, drug dose
zd 4054: DT, drug therapy
zd 4054: PD, pharmacology
zd 4054: PO, oral drug administration
placebo
peptide hydrolase inhibitor: CB, drug combination
peptide hydrolase inhibitor: CM, drug comparison
peptide hydrolase inhibitor: IT, drug interaction
peptide hydrolase inhibitor: DT, drug therapy
peptide hydrolase inhibitor: PD, pharmacology
peptide hydrolase inhibitor: PO, oral drug administration
2 (3 mercaptopropyl)pentanedioic acid: DT, drug therapy
2 (3 mercaptopropyl)pentanedioic acid: PD, pharmacology
2 (3 mercaptopropyl)pentanedioic acid: PO, oral drug administration
nucleoside analog: CT, clinical trial
nucleoside analog: DO, drug dose
nucleoside analog: DT, drug therapy
nucleoside analog: PK, pharmacokinetics
nucleoside analog: PD, pharmacology
nucleoside analog: IV, intravenous drug administration
cp 4055: CT, clinical trial
cp 4055: DO, drug dose
cp 4055: DT, drug therapy
cp 4055: PK, pharmacokinetics
cp 4055: PD, pharmacology
cp 4055: IV, intravenous drug administration
a 800141: CB, drug combination
a 800141: CM, drug comparison
a 800141: IT, drug interaction
a 800141: DT, drug therapy
a 800141: PD, pharmacology
a 800141: PO, oral drug administration
a 849519: CB, drug combination
a 849519: CM, drug comparison
a 849519: DT, drug therapy
a 849519: PD, pharmacology
a 849519: PO, oral drug administration
etoposide: CB, drug combination
etoposide: CM, drug comparison

etoposide: IT, drug interaction
etoposide: DT, drug therapy
etoposide: PD, pharmacology
abt 737: CB, drug combination
abt 737: CM, drug comparison
abt 737: DT, drug therapy
abt 737: PD, pharmacology
ks 119: PD, pharmacology
ks 119w: PD, pharmacology
cg 0070: DO, drug dose
cg 0070: DT, drug therapy
cg 0070: PD, pharmacology
cancer vaccine: AE, adverse drug reaction
cancer vaccine: CT, clinical trial
cancer vaccine: DO, drug dose
cancer vaccine: DT, drug therapy
cancer vaccine: PK, pharmacokinetics
ign 311: AE, adverse drug reaction
ign 311: CT, clinical trial
ign 311: DO, drug dose
ign 311: DT, drug therapy
ign 311: PK, pharmacokinetics
unclassified drug

CAS REGISTRY NO.: (carboplatin) 41575-94-4; (paclitaxel) 33069-62-4; (doxorubicin) 23214-92-8, 25316-40-9; (etoposide) 33419-42-0

CHEMICAL NAME: (1) Dts 201; (2) Dts 201; (3) Zd 4054; (4) Cp 4055; (5) A 849519; (6) A 800141; (7) Abt 737; (8) Abt 737; (9) Ks 119w; (10) Cg 0070; (11) Ign 311

COMPANY NAME: (1) Diatos; (2) Medarex; (3) Astra Zeneca; (4) Clavis Pharma; (7) Abbott; (8) Idun; (9) Vion; (10) Cell Genesys; (11) Igeneon; Agennix; Guilford

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ACCESSION NUMBER: 2005463709 EMBASE Full-text

TITLE: Anticancer therapeutics: "Addictive" targets, multi-targeted drugs, new drug combinations.

AUTHOR: Broxterman H.J.; Georgopapadakou N.H.

CORPORATE SOURCE: H.J. Broxterman, Department of Medical Oncology, Vrije Universiteit Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, Netherlands. H.Broxterman@VUmc.nl

SOURCE: Drug Resistance Updates, (2005) Vol. 8, No. 4, pp. 183-197.
Refs: 168
ISSN: 1368-7646 CODEN: DRUPFW

PUBLISHER IDENT.: S 1368-7646(05)00068-3

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Nov 2005
Last Updated on STN: 28 Nov 2005

ABSTRACT: The annual meeting of the American Association for Cancer Research (AACR) provided a panoramic view of new developments and trends in cancer research. In the area of new drug development, a recurrent theme was receptor

tyrosine kinase (TK) inhibitors, with multitargeted, small molecule inhibitors - highly potent against a family of receptors such as vascular endothelial growth factor receptor (VEGFR), platelet-derived growth factor (PDGFR) and the receptor tyrosine kinase KIT - taking centre stage. Several agents interfering with intracellular targets that are components of key oncogenic signaling pathways, such as RAF kinase, phosphatidylinositol 3-kinase (PI3K)/Akt or Src, are in preclinical and early clinical development. "Addictive" targets, such as the Bcr-Abl fusion protein in chronic myeloid leukemia (CML), are critical for maintaining the malignant phenotype and hence represent an Achilles' heel for selective drugs. Significantly, novel targeted therapeutics currently in clinical development do not generally lead to cures or long-term survival for most intractable cancers; resistance may eventually develop. Anti-metastatic agents and anti-adhesion drugs, which collectively act on tumor cell-stroma interactions (anti-stromal therapy), are also actively pursued. In addition, forms of cell death other than apoptosis - cellular senescence, cancer cell-specific cell-cycle processes and the hypoxic environment - are being explored in order to identify novel targets for more selective therapy. This report also highlights developments aimed at more safe and effective drug combinations. Evaluating drug combinations, and elucidating the rationale for combinations of old (cytotoxic) and new (biological) anticancer agents, are promising research areas and taxane-based combinations are presented as examples. The report is based on presentations at AACR 2005 and related publications of the first half of 2005.

CONTROLLED TERM: Medical Descriptors:
*cancer combination chemotherapy
*antineoplastic activity
*drug targeting
signal transduction
drug mechanism
phenotype
drug research
cancer research
cancer survival
cancer: DR, drug resistance
cancer: DT, drug therapy
cell interaction
drug safety
apoptosis
hypoxia
cell death
stroma
human
nonhuman
clinical trial
conference paper
priority journal

CONTROLLED TERM: Drug Descriptors:
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DV, drug development
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PD, pharmacology
protein tyrosine kinase inhibitor: CM, drug comparison
protein tyrosine kinase inhibitor: DV, drug development
protein tyrosine kinase inhibitor: PD, pharmacology
growth factor receptor
bevacizumab: CB, drug combination
bevacizumab: IT, drug interaction
bevacizumab: PD, pharmacology

doxorubicin: IT, drug interaction
doxorubicin: PD, pharmacology
paclitaxel: CM, drug comparison
paclitaxel: IT, drug interaction
paclitaxel: PR, pharmaceutics
paclitaxel: PD, pharmacology
fluorouracil: IT, drug interaction
fluorouracil: PD, pharmacology
chir 258: DV, drug development
chir 258: DO, drug dose
chir 258: PO, oral drug administration
chir 258: PD, pharmacology
gefitinib: PD, pharmacology
imatinib: PD, pharmacology
5 (5 fluoro 1,2 dihydro 2 oxo 3 indolylidenemethyl) 2,4 dimethyl 1h pyrrole 3 carboxylic acid (2 diethylaminoethyl)amide: PD, pharmacology
cp 673451: DV, drug development
cp 673451: PD, pharmacology
bay 579352: DV, drug development
bay 579352: PD, pharmacology
jnj 17029259: DV, drug development
jnj 17029259: PD, pharmacology
abt 869: CT, clinical trial
abt 869: CM, drug comparison
abt 869: DV, drug development
abt 869: DO, drug dose
abt 869: PO, oral drug administration
abt 869: PD, pharmacology
dasatinib: DV, drug development
dasatinib: PD, pharmacology
sorafenib: DV, drug development
sorafenib: PD, pharmacology
tki 28: DV, drug development
tki 28: DO, drug dose
tki 28: PD, pharmacology
azd 2171: DV, drug development
azd 2171: PD, pharmacology
monoclonal antibody 1m 609: DV, drug development
monoclonal antibody 1m 609: PD, pharmacology
cilengitide: DV, drug development
cilengitide: PD, pharmacology
fumagillol chloroacetylcarbamate: DV, drug development
fumagillol chloroacetylcarbamate: PD, pharmacology
a 800141: DV, drug development
a 800141: PD, pharmacology
azd 0530: DV, drug development
azd 0530: PD, pharmacology
ski 606: DV, drug development
ski 606: PD, pharmacology
1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane): DV, drug development
1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane): PD, pharmacology
bms 188797: CM, drug comparison
bms 188797: DV, drug development
bms 188797: TO, drug toxicity
bms 188797: PD, pharmacology
tl 310: DV, drug development
tl 310: PD, pharmacology

taxane derivative: CB, drug combination
taxane derivative: DV, drug development
taxane derivative: PD, pharmacology
unindexed drug
unclassified drug
bay 57 9352
bms 354825
abraxane
sutent
ag 013736
tipifarnib
lonafarnib
a 443654
zd 4054
n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine
sb 743921
vx 680
pha 680632
on 01910
roscovitine
seliciclib
ks 119w
1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone
bn 82685
fr 901228
n (2 aminophenyl) 4 (3 pyridinylmethoxycarbonylaminomethyl) benzamide
nvp laq 824
mkc 1192
sns 595
ag 14361
zk 304709
chr 2797
cdp 860
ks 119
da 3003 1
nsc 663284
da 30003 1
jun 1111

CAS REGISTRY NO.: (bevacizumab) 216974-75-3; (doxorubicin) 23214-92-8, 25316-40-9; (paclitaxel) 33069-62-4; (fluorouracil) 51-21-8; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (imatinib) 152459-95-5, 220127-57-1; (5 (5 fluoro 1,2 dihydro 2 oxo 3 indolylidenemethyl) 2,4 dimethyl 1h pyrrole 3 carboxylic acid (2 diethylaminoethyl)amide) 557795-19-4; (sorafenib) 284461-73-0; (cilengitide) 188968-51-6; (fumagillol chloroacetylcarbamate) 129298-91-5; (1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane)) 155148-31-5; (tipifarnib) 192185-72-1; (lonafarnib) 193275-84-2; (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine) 156161-89-6; (roscovitine) 186692-46-6; (1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone) 136470-65-0; (fr 901228) 128517-07-7

CHEMICAL NAME: (1) Bay 57 9352; (2) Jnj 17029259; (3) Chir 258; (4) Bms 354825; (5) Abt 869; (6) A 800141; (7) Azd 0530; (8) Ski

606; (9) Abi 007; (10) Abraxane; (11) Zd 1839; (12) Iressa; (13) Sti 571; (14) Gleevec; (15) Su 11248; (16) Sutent; (17) Bms 188797; (18) Taxol; (19) Tl 310; (20) Ag 013736; (21) Zarnestra; (22) Sch 66336; (23) A 443654; (24) Zd 4054; (25) Bq 788; (26) Sb 743921; (27) Vx 680; (28) Pha 680632; (29) On 01910; (30) Cyc 202; (31) Seliciclib; (32) Ks 119w; (33) Aq4n; (34) Bn 82685; (35) Fk 228; (36) Fr 901228; (37) Ms 275; (38) Nvp laq 824; (39) Mkc 1192; (40) Sns 595; (41) Sns 595; (42) Ag 14361; (43) Tki 28; Bay 43 9006; Azd 2171; Zk 304709; Emd 121974; Vitaxin; Chr 2797; Amd 3100; Cp 673451; R 115777; Cdp 860; Ks 119; Da 3003 1; Nsc 663284; Da 30003 1; Jun 1111; Tnp 470

COMPANY NAME: (1) Bayer (Germany); (3) Chiron (United States); (4) Bristol (United States); (8) Wyeth (United States); (10) American BioScience (United States); (16) Sugen pfizer; (18) Bristol Myers Squibb; (19) Taxolog (United States); (20) Agouron pfizer; (21) Johnson and Johnson (United States); (22) Schering Plough (United States); (23) Abbott (United States); (24) Astra Zeneca (United States); (25) Banyu (Japan); (26) Cytokinetics (United States); (27) Vertex (United States); (28) Nerviano Medical Sciences (Italy); (29) Onconova Therapeutics (United States); (31) Cyclacel (United Kingdom); (32) Vion (United States); (33) Novacea (United States); (34) Ipsen (France); (36) Astellas pharma; (37) Mitsui; (38) Novartis (Switzerland); (39) Miikana therapeutics (United States); (40) Dainippon (Japan); (41) Sunesis (United States); (42) Pfizer agouron (United States); (43) Shanghai Institute of Pharmaceutical Industries (China)

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ACCESSION NUMBER: 2005013615 EMBASE Full-text
TITLE: Molecular pathology in oncology - The AstraZeneca perspective.
AUTHOR: Campbell D.A.; Carmichael J.; Chopra R.
CORPORATE SOURCE: D.A. Campbell, Department of Experimental Medicine, AstraZeneca, Alderley Park, Macclesfield, Cheshire SK10 4TG, United Kingdom. david.campbell@astrazeneca.com
SOURCE: Pharmacogenomics, (2004) Vol. 5, No. 8, pp. 1167-1173. .
Refs: 18
ISSN: 1462-2416 CODEN: PARMFL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jan 2005
Last Updated on STN: 20 Jan 2005

ABSTRACT: Growth of the oncology portfolio remains of strategic importance to AstraZeneca, and the adoption of new technologies to allow us to enhance this portfolio is central to this strategy. With the move away from classical hormonal and cytotoxic therapies to the development of more targeted approaches for the treatment of cancer, an understanding of the molecular pathology of the disease state is becoming vital. Our understanding of the pathogenesis of cancer has increased dramatically over the last few decades and with the

publication of the human genome and the resultant explosion in the field of genetics and genomics, AstraZeneca is turning its attention to using these new technologies to enhance the oncology R&D platform. In particular, the fields of pharmacogenetics and pharmacogenomics in relation to oncology have received much attention and this has been mirrored externally both within the pharmaceutical/biotechnology and academic sectors. Future products from the AstraZeneca oncology portfolio will increasingly rely on the use of genetics and genomics for patient identification and stratification, whilst these technologies will also provide a source of novel biomarkers and diagnostics that may allow us to streamline the R&D process and help us to better understand the biological basis of the diseases we are aiming to treat. The AstraZeneca perspective is, however, pragmatic enough to appreciate the practical challenges involved in applying pharmacogenetics and genomics not only for early drug development, but also in the organization of the healthcare infrastructure to undertake timely and complex laboratory investigations. Finally, validation of this approach will require carefully controlled clinical studies. .COPYRGT. 2004 Future Medicine Ltd.

CONTROLLED TERM: Medical Descriptors:
*carcinogenesis
*cancer therapy
drug industry
medical technology
hormonal therapy
cytotoxicity
molecular mechanics
human genome
genome analysis
pharmacogenetics
pharmacogenomics
validation process
drug targeting
drug mechanism
gene expression profiling
proteomics
histopathology
drug response
acute lymphoblastic leukemia: ET, etiology
human
clinical trial
article
Drug Descriptors:
biological marker: EC, endogenous compound
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: DV, drug development
angiogenesis inhibitor: PD, pharmacology
azd 2171: CT, clinical trial
azd 2171: DV, drug development
azd 9935: CT, clinical trial
azd 9935: DV, drug development
azd 4440: DV, drug development
zd 4054: CT, clinical trial
zd 4054: DV, drug development
zd 4054: PD, pharmacology
azd 0530: CT, clinical trial
azd 0530: DV, drug development
azd 0424: CT, clinical trial
azd 0424: DV, drug development
azd 3409: CT, clinical trial
azd 5438: CT, clinical trial

n (4 bromo 2 fluorophenyl) 6 methoxy 7 (1 methyl 4 piperidinylmethoxy) 4 quinazolinamine: CT, clinical trial
n (4 bromo 2 fluorophenyl) 6 methoxy 7 (1 methyl 4 piperidinylmethoxy) 4 quinazolinamine: DV, drug development
phosphotransferase inhibitor: CT, clinical trial
phosphotransferase inhibitor: DV, drug development
azd 1152: CT, clinical trial
azd 1152: DV, drug development
mitogen activated protein kinase inhibitor: CT, clinical trial
mitogen activated protein kinase inhibitor: DV, drug development
azd 6244: CT, clinical trial
azd 6244: DV, drug development
imatinib: PD, pharmacology
epidermal growth factor receptor: EC, endogenous compound
epidermal growth factor receptor kinase inhibitor: PD, pharmacology
gefitinib: PD, pharmacology
epidermal growth factor receptor 2: EC, endogenous compound
trastuzumab
estrogen receptor: EC, endogenous compound
cyclin dependent kinase inhibitor: CT, clinical trial
cyclin dependent kinase inhibitor: DV, drug development
epidermal growth factor receptor kinase: EC, endogenous compound
phosphotransferase: EC, endogenous compound
paraffin
Abelson kinase: EC, endogenous compound
endothelin A receptor antagonist: CT, clinical trial
endothelin A receptor antagonist: DV, drug development
endothelin A receptor: EC, endogenous compound
unindexed drug
unclassified drug

CAS REGISTRY NO.: (n (4 bromo 2 fluorophenyl) 6 methoxy 7 (1 methyl 4 piperidinylmethoxy) 4 quinazolinamine) 443913-73-3; (imatinib) 152459-95-5, 220127-57-1; (gefitinib) 184475-35-2, 184475-55-6, 184475-56-7; (epidermal growth factor receptor 2) 137632-09-8; (trastuzumab) 180288-69-1; (epidermal growth factor receptor kinase) 79079-06-4; (phosphotransferase) 9031-09-8, 9031-44-1

CHEMICAL NAME: (1) Azd 2171; (2) Zd 6474; (3) Azd 9935; (4) Azd 4440; (5) Zd 4054; (6) Azd 0530; (7) Azd 0424; (8) Azd 3409; (9) Azd 5438; (10) Azd 6244; (11) Azd 1152

COMPANY NAME: (11) Astra Zeneca

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ACCESSION NUMBER: 2005014847 EMBASE Full-text

TITLE: Newer therapies in advanced prostate cancer.

AUTHOR: Hegeman R.B.; Liu G.; Wilding G.; McNeel D.G.

CORPORATE SOURCE: Dr. D.G. McNeel, Department of Medicine, Univ. of WI Compreh. Cancer Center, K4/518 Clinical Science Center, 600 Highland Ave, Madison, WI 53792, United States. dm3@medicine.wisc.edu

SOURCE: Clinical Prostate Cancer, (2004) Vol. 3, No. 3, pp. 150-156. .
Refs: 66
ISSN: 1540-0352 CODEN: CPCLC4

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jan 2005
Last Updated on STN: 20 Jan 2005

ABSTRACT: Prostate cancer is a leading cause of morbidity and mortality among males. Androgen ablation as initial therapy for advanced prostate cancer provides high response rates but does not cure disease, as nearly all men with metastases will eventually progress to hormone-refractory prostate cancer (HRPC). Present chemotherapy regimens for HRPC can provide palliation and have recently demonstrated an increase in overall survival. Over the past 2 decades, these regimens represent clear advances in the treatment of metastatic prostate cancer but also demonstrate that newer therapies are needed. Studies are ongoing to provide viable alternatives among traditional cytotoxic therapies as well as among novel agents targeting specific molecular pathways. This article reviews some of the newer therapies being developed and evaluated, including the epothilone analogues, human epidermal growth factor receptor pathway inhibitors, angiogenesis inhibitors, and endothelin receptor antagonists.

CONTROLLED TERM: Medical Descriptors:
*prostate cancer: DT, drug therapy
cancer chemotherapy
cause of death
cancer palliative therapy
metastasis: CO, complication
cancer survival
gene overexpression
side effect: SI, side effect
neutropenia: SI, side effect
febrile neutropenia: SI, side effect
sensory neuropathy: SI, side effect
nausea: SI, side effect
vomiting: SI, side effect
diarrhea: SI, side effect
visual hallucination: SI, side effect
fatigue: SI, side effect
abdominal pain: SI, side effect
anemia: SI, side effect
gastrointestinal hemorrhage: SI, side effect
esophagus varices: SI, side effect
heart left ventricle failure: SI, side effect
heart infarction: SI, side effect
hypoalbuminemia: SI, side effect
angioneurotic edema: SI, side effect
liver toxicity: SI, side effect
rhinitis: SI, side effect
asthenia: SI, side effect
headache: SI, side effect
peripheral edema: SI, side effect
cell line
neuropathy: SI, side effect
human
clinical trial
review

CONTROLLED TERM: Drug Descriptors:
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: CM, drug comparison
*antineoplastic agent: DT, drug therapy
*antineoplastic agent: PD, pharmacology
epothilone derivative: CT, clinical trial
epothilone derivative: AN, drug analysis
epothilone derivative: CM, drug comparison
epothilone derivative: DT, drug therapy
epothilone derivative: IV, intravenous drug administration
epothilone derivative: PD, pharmacology
angiogenesis inhibitor: AE, adverse drug reaction
angiogenesis inhibitor: CT, clinical trial
angiogenesis inhibitor: CB, drug combination
angiogenesis inhibitor: DT, drug therapy
angiogenesis inhibitor: PD, pharmacology
endothelin receptor antagonist: AE, adverse drug reaction
endothelin receptor antagonist: CT, clinical trial
endothelin receptor antagonist: DO, drug dose
endothelin receptor antagonist: DT, drug therapy
endothelin receptor antagonist: PO, oral drug administration
endothelin receptor antagonist: PD, pharmacology
zd 4054: DT, drug therapy
zd 4054: PO, oral drug administration
zd 4054: PD, pharmacology
atrasentan: AE, adverse drug reaction
atrasentan: CT, clinical trial
atrasentan: DO, drug dose
atrasentan: DT, drug therapy
atrasentan: PO, oral drug administration
atrasentan: PD, pharmacology
prinomastat: CT, clinical trial
prinomastat: CB, drug combination
prinomastat: DT, drug therapy
prinomastat: PD, pharmacology
ixabepilone: AE, adverse drug reaction
ixabepilone: CT, clinical trial
ixabepilone: AN, drug analysis
ixabepilone: CB, drug combination
ixabepilone: CM, drug comparison
ixabepilone: DT, drug therapy
ixabepilone: IV, intravenous drug administration
ixabepilone: PD, pharmacology
cetuximab: CT, clinical trial
cetuximab: CB, drug combination
cetuximab: DT, drug therapy
cetuximab: PD, pharmacology
doxorubicin: CT, clinical trial
doxorubicin: CB, drug combination
doxorubicin: DT, drug therapy
doxorubicin: PD, pharmacology
trastuzumab: CT, clinical trial
trastuzumab: CB, drug combination
trastuzumab: DT, drug therapy
trastuzumab: PD, pharmacology
pertuzumab: AE, adverse drug reaction
pertuzumab: CT, clinical trial

pertuzumab: DO, drug dose
pertuzumab: DT, drug therapy
pertuzumab: IV, intravenous drug administration
pertuzumab: PD, pharmacology
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: CM, drug comparison
mitoxantrone: DT, drug therapy
mitoxantrone: PD, pharmacology
taxane derivative: AN, drug analysis
taxane derivative: CM, drug comparison
taxane derivative: DT, drug therapy
taxane derivative: PD, pharmacology
epothilone B: AE, adverse drug reaction
epothilone B: CT, clinical trial
epothilone B: CB, drug combination
epothilone B: DT, drug therapy
epothilone B: PD, pharmacology
estramustine: AE, adverse drug reaction
estramustine: CT, clinical trial
estramustine: CB, drug combination
estramustine: CM, drug comparison
estramustine: DT, drug therapy
estramustine: PO, oral drug administration
estramustine: PD, pharmacology
prostate specific antigen: EC, endogenous compound
prednisone: CT, clinical trial
prednisone: CB, drug combination
prednisone: CM, drug comparison
prednisone: DT, drug therapy
prednisone: PD, pharmacology
d 2163: CT, clinical trial
d 2163: CB, drug combination
d 2163: DT, drug therapy
2 methoxyestradiol: AE, adverse drug reaction
2 methoxyestradiol: CT, clinical trial
2 methoxyestradiol: DT, drug therapy
2 methoxyestradiol: PO, oral drug administration
2 methoxyestradiol: PD, pharmacology
paclitaxel
matrix metalloproteinase inhibitor: AE, adverse drug reaction
matrix metalloproteinase inhibitor: CT, clinical trial
matrix metalloproteinase inhibitor: CB, drug combination
matrix metalloproteinase inhibitor: DT, drug therapy
matrix metalloproteinase inhibitor: PD, pharmacology
epothilone D: AE, adverse drug reaction
epothilone D: CT, clinical trial
epothilone D: DT, drug therapy
epothilone D: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8; (prinomastat) 192329-42-3, 195008-93-6; (ixabepilone) 219989-84-1; (cetuximab) 205923-56-4; (doxorubicin) 23214-92-8, 25316-40-9; (trastuzumab) 180288-69-1; (mitoxantrone) 65271-80-9, 70476-82-3; (epothilone B) 152044-54-7; (estramustine) 2998-57-4, 62899-40-5; (prednisone) 53-03-2; (d 2163) 191537-76-5; (2 methoxyestradiol) 362-07-2; (paclitaxel) 33069-62-4

CHEMICAL NAME: (1) Zd 4054; Bms 247550; Kos 862; Bms 275291

COMPANY NAME: (1) Astra Zeneca

L12 ANSWER 33 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005147012 EMBASE Full-text

TITLE: [Pathophysiology and new therapeutic strategies for bone metastases of prostate cancer: The sick-bed laboratory]. PHYSIOPATHOLOGIE ET NOUVELLES STRATEGIES THERAPEUTIQUES DES METASTASES OSSEUSES DU CANCER DE LA PROSTATE: DU LABORATOIRE AU LIT DU MALADE.

AUTHOR: Tombal B.; Tajeddine N.; Machiels J.-P.; Van Cangh P.-J.

CORPORATE SOURCE: Dr. B. Tombal, Service d'Urologie, Cliniques Universitaire Saint-Luc, avenue Hippocrate 10, B-1200 Bruxelles, Belgium. bertrand.tombal@fymu.ucl.ac.be

SOURCE: Louvain Medical, (2004) Vol. 123, No. 4, pp. S172-S179.
Refs: 32
ISSN: 0024-6956 CODEN: LOMEAL

COUNTRY: Belgium
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: French
ENTRY DATE: Entered STN: 28 Apr 2005
Last Updated on STN: 28 Apr 2005

CONTROLLED TERM: Medical Descriptors:
*bone metastasis: CO, complication
*bone metastasis: DI, diagnosis
*bone metastasis: DT, drug therapy
*bone metastasis: PC, prevention
*prostate carcinoma
*laboratory test
pathophysiology
cancer therapy
cancer diagnosis
fracture: CO, complication
osteoclast
cell kinetics
osteoblast
drug mechanism
human
male
clinical trial
systematic review
conference paper
Drug Descriptors:
zoledronic acid: CT, clinical trial
zoledronic acid: DT, drug therapy
zoledronic acid: PD, pharmacology
clodronic acid: CT, clinical trial
clodronic acid: DT, drug therapy
clodronic acid: PD, pharmacology
ibandronic acid: CT, clinical trial
ibandronic acid: DT, drug therapy
ibandronic acid: PD, pharmacology
atrasentan: CT, clinical trial
atrasentan: DT, drug therapy
atrasentan: PD, pharmacology

endothelin receptor affecting agent: CT, clinical trial
endothelin receptor affecting agent: DT, drug therapy
endothelin receptor affecting agent: PD, pharmacology
ym 598: CT, clinical trial
ym 598: DT, drug therapy
ym 598: PD, pharmacology
zd 4054: CT, clinical trial
zd 4054: DT, drug therapy
zd 4054: PD, pharmacology
amgn 007: CT, clinical trial
amgn 007: DT, drug therapy
amgn 007: PD, pharmacology
amg 162: CT, clinical trial
amg 162: DT, drug therapy
amg 162: PD, pharmacology
unclassified drug

CAS REGISTRY NO.: (zoledronic acid) 118072-93-8, 131654-46-1, 165800-06-6, 165800-07-7; (clodronic acid) 10596-23-3, 22560-50-5; (ibandronic acid) 114084-78-5, 138844-81-2, 138926-19-9; (atrasentan) 173864-34-1, 173937-91-2, 195733-43-8

CHEMICAL NAME: (1) Zometa; (2) Bonefos; (3) Ym 598; (4) Zd 4054; (5) Amgn 007; (6) Amg 162

COMPANY NAME: (1) Novartis; (2) Schering AG; (3) Yamanouchi; (4) Astra Zeneca; (6) Amgen; Chugai; Hoffmann La Roche; Abbott

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ACCESSION NUMBER: 2000301562 EMBASE Full-text

TITLE: Endothelin receptor antagonists: A clinical study update.

AUTHOR: Wu-Wong J.R.; Padley R.

CORPORATE SOURCE: J.R. Wu-Wong, Abbott Laboratories, 5440 Patrick Henry Drive, Santa Clara, CA 95054, United States. ruth.r.wuwong@abbott.com

SOURCE: Current Opinion in Cardiovascular, Pulmonary and Renal Investigational Drugs, (2000) Vol. 2, No. 4, pp. 339-344. Refs: 44
ISSN: 1464-8482 CODEN: CCPRFX

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 039 Pharmacy
038 Adverse Reactions Titles
037 Drug Literature Index
030 Pharmacology
028 Urology and Nephrology
018 Cardiovascular Diseases and Cardiovascular Surgery
016 Cancer
015 Chest Diseases, Thoracic Surgery and Tuberculosis
008 Neurology and Neurosurgery

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Sep 2000
Last Updated on STN: 14 Sep 2000

CONTROLLED TERM: Medical Descriptors:
human
clinical trial
drug safety
drug tolerability
drug clearance
prostate cancer: DT, drug therapy
prostate cancer: ET, etiology
hypertension: DT, drug therapy

hypertension: ET, etiology
congestive heart failure: DT, drug therapy
congestive heart failure: ET, etiology
pulmonary hypertension: DT, drug therapy
pulmonary hypertension: ET, etiology
acute kidney failure: DT, drug therapy
acute kidney failure: ET, etiology
subarachnoid hemorrhage: DT, drug therapy
subarachnoid hemorrhage: ET, etiology
stroke: DT, drug therapy
stroke: ET, etiology
chronic obstructive lung disease: DT, drug therapy
chronic obstructive lung disease: ET, etiology
heart infarction: DT, drug therapy
heart infarction: ET, etiology
brain ischemia: DT, drug therapy
brain ischemia: ET, etiology
rhinitis: DT, drug therapy
rhinitis: SI, side effect
disease course
dose response
metabolic disorder: DT, drug therapy
metabolic disorder: SI, side effect
drug formulation
cancer: ET, etiology
cancer: DT, drug therapy
drug selectivity
drug mechanism
drug antagonism
review

CONTROLLED TERM: Drug Descriptors:
*endothelin receptor antagonist: DT, drug therapy
*endothelin receptor antagonist: CT, clinical trial
*endothelin receptor antagonist: DO, drug dose
*endothelin receptor antagonist: CM, drug comparison
*endothelin receptor antagonist: CB, drug combination
*endothelin receptor antagonist: AE, adverse drug reaction
*endothelin receptor antagonist: PR, pharmaceutics
*endothelin receptor antagonist: PO, oral drug administration
*endothelin receptor antagonist: IV, intravenous drug administration
*endothelin receptor antagonist: PK, pharmacokinetics
*endothelin receptor antagonist: PD, pharmacology
*endothelin receptor: EC, endogenous compound
abt 627: DT, drug therapy
abt 627: CT, clinical trial
abt 627: PO, oral drug administration
abt 627: PK, pharmacokinetics
abt 627: DO, drug dose
abt 627: PR, pharmaceutics
abt 627: PD, pharmacology
abt 627: AE, adverse drug reaction
2 (4,6 dimethoxy 2 pyrimidinyloxy) 3 methoxy 3,3 diphenylpropionic acid: DT, drug therapy
2 (4,6 dimethoxy 2 pyrimidinyloxy) 3 methoxy 3,3 diphenylpropionic acid: CT, clinical trial
2 (4,6 dimethoxy 2 pyrimidinyloxy) 3 methoxy 3,3 diphenylpropionic acid: DO, drug dose
2 (4,6 dimethoxy 2 pyrimidinyloxy) 3 methoxy 3,3

diphenylpropionic acid: PO, oral drug administration
2 (4,6 dimethoxy 2 pyrimidinyloxy) 3 methoxy 3,3 diphenylpropionic acid: PD, pharmacology
bosentan: DT, drug therapy
bosentan: CT, clinical trial
bosentan: DO, drug dose
bosentan: CM, drug comparison
bosentan: CB, drug combination
bosentan: PO, oral drug administration
bosentan: AE, adverse drug reaction
bosentan: PD, pharmacology
3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid: DT, drug therapy
3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid: CT, clinical trial
3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid: IV, intravenous drug administration
3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid: PD, pharmacology
enrasentan: DT, drug therapy
enrasentan: CT, clinical trial
enrasentan: PO, oral drug administration
enrasentan: PD, pharmacology
tak 044: DT, drug therapy
tak 044: CT, clinical trial
tak 044: PD, pharmacology
n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide: DT, drug therapy
n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide: CT, clinical trial
n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide: PO, oral drug administration
n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide: DO, drug dose
n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide: IV, intravenous drug administration
n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide: PD, pharmacology
3 [4 [3 (3 methoxy 5 methyl 2 pyrazinylsulfamoyl) 2 pyridyl]phenyl] 2,2 dimethylpropionic acid: DT, drug therapy
3 [4 [3 (3 methoxy 5 methyl 2 pyrazinylsulfamoyl) 2 pyridyl]phenyl] 2,2 dimethylpropionic acid: CT, clinical trial
3 [4 [3 (3 methoxy 5 methyl 2 pyrazinylsulfamoyl) 2 pyridyl]phenyl] 2,2 dimethylpropionic acid: PO, oral drug administration
3 [4 [3 (3 methoxy 5 methyl 2 pyrazinylsulfamoyl) 2 pyridyl]phenyl] 2,2 dimethylpropionic acid: PD, pharmacology

2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid: DT, drug therapy
2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid: CT, clinical trial
2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid: IV, intravenous drug administration
2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid: PD, pharmacology
abt 546: DT, drug therapy
abt 546: CT, clinical trial
abt 546: PO, oral drug administration
abt 546: AE, adverse drug reaction
abt 546: PD, pharmacology
2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine: DT, drug therapy
2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine: CT, clinical trial
2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine: PO, oral drug administration
2 butyl 7 [2 (2 carboxypropyl) 4 methoxyphenyl] 5 (3,4 methylenedioxyphenyl)cyclopenteno[1,2 b]pyridine: PD, pharmacology
bms 193884: DT, drug therapy
bms 193884: CT, clinical trial
bms 193884: PO, oral drug administration
bms 193884: PD, pharmacology
bms 207940: DT, drug therapy
bms 207940: CT, clinical trial
bms 207940: PO, oral drug administration
bms 207940: PD, pharmacology
tezosentan: DT, drug therapy
tezosentan: CT, clinical trial
tezosentan: IV, intravenous drug administration
tezosentan: PD, pharmacology
vml 588: DT, drug therapy
vml 588: CT, clinical trial
vml 588: IV, intravenous drug administration
vml 588: PD, pharmacology
27 o 3 [2 (3 carboxyacryloylamino) 5 hydroxyphenyl]acryloyloxy myricerone: DT, drug therapy
27 o 3 [2 (3 carboxyacryloylamino) 5 hydroxyphenyl]acryloyloxy myricerone: CT, clinical trial
27 o 3 [2 (3 carboxyacryloylamino) 5 hydroxyphenyl]acryloyloxy myricerone: IV, intravenous drug administration
27 o 3 [2 (3 carboxyacryloylamino) 5 hydroxyphenyl]acryloyloxy myricerone: PD, pharmacology
cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl): DT, drug therapy

cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl): CT, clinical trial
cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl): PD, pharmacology
zd 4054: DT, drug therapy
zd 4054: CT, clinical trial
zd 4054: PD, pharmacology
zd 2574: DT, drug therapy
zd 2574: CT, clinical trial
zd 2574: PD, pharmacology
enalapril: DT, drug therapy
enalapril: CM, drug comparison
enalapril: PD, pharmacology
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
cyclosporin A: DT, drug therapy
cyclosporin A: CB, drug combination
cyclosporin A: PD, pharmacology
atrasentan: DT, drug therapy
atrasentan: PD, pharmacology
atrasentan: CT, clinical trial
atrasentan: PO, oral drug administration
darusentan: DT, drug therapy
darusentan: PD, pharmacology
darusentan: CT, clinical trial
darusentan: PO, oral drug administration
sitaxsentan: DT, drug therapy
sitaxsentan: PD, pharmacology
sitaxsentan: CT, clinical trial
sitaxsentan: PO, oral drug administration
sitaxsentan: IV, intravenous drug administration
ro 61 0612: DT, drug therapy
ro 61 0612: PD, pharmacology
ro 61 0612: CT, clinical trial
ro 61 0612: IV, intravenous drug administration
ro 61 1790: DT, drug therapy
ro 61 1790: PD, pharmacology
ro 61 1790: CT, clinical trial
ro 61 1790: IV, intravenous drug administration
unindexed drug
unclassified drug

CAS REGISTRY NO.: (abt 627) 173937-91-2; (2 (4,6 dimethoxy 2 pyrimidinyloxy) 3 methoxy 3,3 diphenylpropionic acid) 171714-84-4; (3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid) 150355-66-1, 157659-79-5; (enrasentan) 167256-08-8, 183507-63-3; (tak 044) 157380-72-8; (n (4 chloro 3 methyl 5 isoxazolyl) 2 [(6 methyl 1,3 benzodioxol 5 yl)acetyl] 3 thiophenesulfonamide) 184036-34-8; (2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid) 142375-60-8; (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)) 136553-81-6; (enalapril) 75847-73-3; (cyclosporin A) 59865-13-3, 63798-73-2

CHEMICAL NAME: (1) Abt 546; (2) Abt 627; (3) J 104132; (4) Bq 123; (5) J 104132; (6) Bms 193884; (7) Bms 207940; (8) Lu 135252; (9) Lu 135252; (10) Vml 588; (11) Ro 47 0203; (12) Ro 61 0612; (13) Ro 61 1790; (14) Vml 588; (15) Ro 61 1790; (16) S

0139; (17) Sb 209670; (18) Sb 217242; (19) Tak 044; (20) Tbc 11251; (21) Zd 1611; (22) Zd 4054; (23) Zd 2574; (24) Fr 139317; (25) Ro 47 0203; (26) Ro 61 1790

COMPANY NAME: (2) Abbott; (4) Banyu; (5) Merck; (7) Bristol Myers Squibb; (8) Knoll; (9) Hoechst Marion Roussel; (13) Hoffmann La Roche; (15) Vanguard; (16) Shionogi; (18) SmithKline Beecham; (19) Takeda; (20) Texas Biotechnology; (23) Astra Zeneca; (24) Fujisawa; (26) Actelion

L12 ANSWER 35 OF 39 ADISCTI COPYRIGHT (C) 2007 Adis Data Information BV on STN

ACCESSION NUMBER: 2006:21716 ADISCTI
DOCUMENT NUMBER: 700012848
TITLE: ADIS TITLE: AZD 4054: adverse reactions Various toxicities Phase II trial in patients patients with metastatic prostate cancer
DOCUMENT TYPE: Ongoing Trial
ADIS REC. CREATED: 30 Mar 2006
ADIS LAST UPDATE: 19 May 2006
REFERENCE: Oncology; Men's Health
1.) ClinicalTrials.gov: US National Institutes of Health
2.) AstraZeneca
LANGUAGE: English
WORD COUNT: 65
OTHER SOURCE: ADISINSIGHT 1998008705
ENTRY DATE: Entered STN: 12 Jun 2006
Last Updated on STN: 12 Jun 2006
ONGOING TRIAL COMNT: Ongoing Trial Comment: This trial is entitled "A phase IIa. open-label, multicenter, dose-escalation study to assess the tolerability and pharmacokinetics of ZD4054 [AZD 4054] given orally once daily in subjects with metastatic prostate cancer".

TEXT - Subject Details:
Type: patients
Location: USA
Disease: Various-toxicities
Patient Inclusion: prostate cancer with bone metastases
Patient Exclusion: >2 prior chemotherapy regimens; radiotherapy, chemotherapy or bisphosphonates within the past four weeks
TEXT - Age Key: adult
TEXT - Study Details:
Status: in progress
Design: multicentre, prospective
Control: baseline comparison
Phase: II
Endpoints: Pharmacokinetic-parameters
Companies: AstraZeneca, AstraZeneca
ID: 4054IL0004 (AstraZeneca)
700012848 (Clinical Trials Insight)
NCT00055471 (ClinicalTrials.gov: US National Institutes of Health)

CONTROLLED TERM: Drug Descriptors: AZD 4054, adverse reactions
CONTROLLED TERM: Disease Descriptors: Various toxicities, drug induced

L12 ANSWER 36 OF 39 ADISCTI COPYRIGHT (C) 2007 Adis Data Information BV on

STN
ACCESSION NUMBER: 2006:14987 ADISCTI
DOCUMENT NUMBER: 700005088
TITLE: ADIS TITLE: AZD 40554: therapeutic use
Prostate cancer, bone metastases
A phase II study in patients with hormone-refractory adenocarcinoma
DOCUMENT TYPE: Ongoing Trial
ADIS REC. CREATED: 12 Oct 2005
ADIS LAST UPDATE: 25 Jul 2006
REFERENCE: Oncology; Men's Health; PharmacoEconomics
1.) National Research Register: National Health Service
2.) ClinicalTrials.gov: US National Institutes of Health
3.) AstraZeneca
LANGUAGE: English
WORD COUNT: 183
OTHER SOURCE: ADISINSIGHT 1998008705; ADISINSIGHT 2000000910
ENTRY DATE: Entered STN: 12 Jun 2006
Last Updated on STN: 12 Jun 2006
ONGOING TRIAL COMNT: Ongoing Trial Comment: This trial, entitled "Phase II randomized study of ZD4054 [AZD 4054] in patients with hormone-refractory prostate cancer and bone metastases", will compare the efficacy, tolerability, pharmacokinetics, pharmacodynamics and quality-of-life effects of differing doses of AZD 4054 with that of placebo.

TEXT - Subject Details:
Type: patients
Planned No: 260
Location: Australia, Belgium, Canada, Denmark, England, Finland, France, Indonesia, Multinational, Netherlands, Norway, Poland, Sweden, Switzerland, USA
Disease: Cancer-metastases, Prostate-cancer
Patient Inclusion: metastatic, hormone-refractory adenocarcinoma, evidence of bone metastases, <75% disease involvement of spine, pelvis or ribs, no pain or controlled pain, rising prostate specific antigen, surgically castrated or continuously medically castrated, ineligible for or refused standard chemotherapy, WHO performance status of 0-1
Patient Exclusion: CNS metastasis, neurologic signs or symptoms of acute or evolving spinal cord compression, prior cytotoxic chemotherapy or endothelin-receptor antagonists
TEXT - Age Key: adult
TEXT - Study Details:
Status: recruiting
Design: double-blind, multicentre, parallel, randomised
Control: baseline comparison, drug dosage comparison, placebo comparison
Phase: II
Endpoints: Biomarker-levels, Endothelin-1-levels, Objective-clinical-response-rate, Pain-relief, Pharmacokinetic-parameters, Prostate-specific-antigen, Prostate-specific-antigen-response, Prostate-specific-antigen-response-rate, Quality-of-life, Recommended-dose, Survival, Time-to-disease-progression
Study Center: Jonsson Comprehensive Cancer Center
Companies: AstraZeneca, AstraZeneca
ID: 04MRE08-22 (Multi-Centre Research Ethics Committee)
700005088 (Clinical Trials Insight)
CDR0000422433 (National Cancer Institute)
D4320C00006 (AstraZeneca)
N0285169321 (National Research Register: National Health Service)

NCT00090363 (ClinicalTrials.gov: US National Institutes of Health)
NCT00107146 (ClinicalTrials.gov: US National Institutes of Health)
UCLA0407043-01 (University of California, Los Angeles)
ZD4054 (AstraZeneca)
ZENECA4054IL0006 (AstraZeneca)
ZENECAD4320C00006 (AstraZeneca)

CONTROLLED TERM: Drug Descriptors: AZD 4054, therapeutic use
CONTROLLED TERM: Disease Descriptors: Cancer metastases, treatment; Prostate cancer, treatment
CONTROLLED TERM: Pharmacoeconomic Descriptors: Quality of life

L12 ANSWER 37 OF 39 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:880051 SCISEARCH Full-text
THE GENUINE ARTICLE: 943BK
TITLE: Tolerability profile of ZD4054 is consistent with the effects of endothelin A receptor-specific antagonism
AUTHOR: Liu G (Reprint); Dreicer R; Hou J; Chen Y; Wilding G
CORPORATE SOURCE: Univ Wisconsin, Madison, WI 53706 USA; Cleveland Clin Fdn, Cleveland, OH 44195 USA; AstraZeneca Pharmaceut, Wilmington, DE USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF CLINICAL ONCOLOGY, (1 JUN 2005) Vol. 23, No. 16, Part 1, Supp. [S], pp. 409S-409S.
ISSN: 0732-183X.
PUBLISHER: AMER SOC CLINICAL ONCOLOGY, 330 JOHN CARLYLE ST, STE 300, ALEXANDRIA, VA 22314 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 8 Sep 2005
Last Updated on STN: 8 Sep 2005
CATEGORY: ONCOLOGY

L12 ANSWER 38 OF 39 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:871085 SCISEARCH Full-text
THE GENUINE ARTICLE: 858UD
TITLE: N-(3-methoxy-5-methylpyrazin-2-yl)-2-[4-(1,3,4-oxadiazol-2-yl)phenyl]pyridine-3-sulfonamide (ZD4054 form 1)
AUTHOR: Stensland B (Reprint); Roberts R J
CORPORATE SOURCE: AstraZeneca, Preformulat & Biopharmaceut, Solid State Anal & Phys Chem, PAR&D-SBBG B341-3, SE-15185 Sodertalje, Sweden (Reprint); AstraZeneca, Preformulat & Biopharmaceut, Solid State Anal & Phys Chem, SE-15185 Sodertalje, Sweden; AstraZeneca, Preformulat & Biopharmaceut, PAR&D, Macclesfield SK10 2NA, Cheshire, England
birgitta.stensland@astrazeneca.com
COUNTRY OF AUTHOR: Sweden; England
SOURCE: ACTA CRYSTALLOGRAPHICA SECTION E-STRUCTURE REPORTS ONLINE, (OCT 2004) Vol. 60, Part 10, pp. O1817-O1819.
ISSN: 1600-5368.
PUBLISHER: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK.
DOCUMENT TYPE: Article; Journal

LANGUAGE: English
REFERENCE COUNT: 10
ENTRY DATE: Entered STN: 29 Oct 2004
Last Updated on STN: 29 Oct 2004

ABSTRACT:
The title compound, C19H16N6O4S, crystallizes from N-methylpyridine in the centrosymmetric space group P2(1)/n with four molecules in the unit cell. The molecule has 11 heteroatoms, of which only one is protonated. This potential hydrogen-bond donor, viz. the NH amide group, participates in both intra- and intermolecular hydrogen-bond interactions, thus contributing to the stabilization of the molecular conformation and the linking of molecules as dimers. The hairpin-like folded molecule is arranged with three of its four aromatic rings in two parallel planes intersected by a sulfonamide moiety. In this way, the molecules stack efficiently, facilitated by short-range van der Waals forces. No residual volume for solvent inclusion was found.

CATEGORY: CRYSTALLOGRAPHY
REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	ARN PG (RPG)	Referenced Work (RWK)
*NON BV	2000			KAPPACCD SERV SOFTW
ADSMOND D A	2001	90	2058	J PHARM SCI
ALTOMARE A	1992			SIR92 PROGRAM CRYSTA
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L12 ANSWER 39 OF 39 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:446254 SCISEARCH Full-text
THE GENUINE ARTICLE: 626VZ
TITLE: ZD4054: a specific endothelin A receptor antagonist with potential utility in prostate cancer and metastatic bone disease
AUTHOR: Curwen J O (Reprint); Wilson C
CORPORATE SOURCE: AstraZeneca, Canc & Infect Biosci, Macclesfield, Cheshire, England
COUNTRY OF AUTHOR: England
SOURCE: EUROPEAN JOURNAL OF CANCER, (NOV 2002) Vol. 38, Supp. [7], pp. S102-S102. MA 340.
ISSN: 0959-8049.
PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 13 Jun 2003
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SEARCH HISTORY

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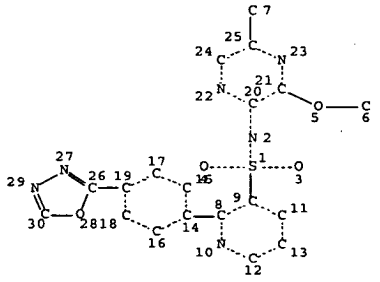

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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE
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L1 1 SEA ABB=ON US2006-569583/AP
D SCAN
SEL RN
SAVE TEMP L1 HA583CAAU/A

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L9            35 DUP REM L8 (11 DUPLICATES REMOVED)
                    ANSWERS '1-15' FROM FILE CAPLUS
                    ANSWERS '16-25' FROM FILE USPATFULL
                    ANSWERS '26-32' FROM FILE IMSDRUGNEWS
                    ANSWER '33' FROM FILE IMSRESEARCH
                    ANSWER '34' FROM FILE PROUSDDR
                    ANSWER '35' FROM FILE SYNTHLINE
                D IBIB ED ABS HITRN 1-16
                D IBIB ED ABS HITRN 17-25
                D IALL 26-35

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS,
     BIBLIODATA, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CAOLD, CAPLUS, CASREACT, CBNB, CEABA-VTB, CERAB, ...' ENTERED AT 16:11:24
     ON 01 FEB 2007
              SEA ZIBOTENTAN# OR ZD4054 OR ZD 4054
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               4   FILE BIOSIS
              11   FILE CAPLUS
              12   FILE DDFU
              12   FILE DRUGU
              19   FILE EMBASE
               3   FILE ESBIOBASE
               3   FILE IFIPAT
               7   FILE IMSDRUGNEWS
               3   FILE MEDLINE
               2   FILE NLDB
               2   FILE PASCAL
              43   FILE PCTFULL
               1   FILE PHARMAML
               7   FILE PHIN
              10   FILE PROMT
               7   FILE SCISEARCH
               1   FILE SYNTHLINE
               8   FILE TOXCENTER
              17   FILE USPATFULL
               3   FILE WPIDS
               3   FILE WPINDEX
L10            QUE ABB=ON  ZIBOTENTAN# OR ZD4054 OR ZD 4054
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L12           39 DUP REM L11 (17 DUPLICATES REMOVED)
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                    ANSWER '14' FROM FILE PASCAL
                    ANSWERS '15-17' FROM FILE WPIX
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                    ANSWER '20' FROM FILE ESBIOBASE
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                    ANSWERS '35-36' FROM FILE ADISCTI
                    ANSWERS '37-39' FROM FILE SCISEARCH
                D IALL 1-14
                D IALL ABEQ TECH 15-17
                D IALL 18-39

     FILE 'HOME' ENTERED AT 16:31:35 ON 01 FEB 2007

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